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VOL. 70 AUGUST, 1955 NO. 2

Original Communications

FOREIGN BODIES LOST IN THE PELVIS DURING ATTEMPTED ABORTION WITH SPECIAL REFERENCE TO URETHRAL CATHETERS

DAVID ZAKIN, M.D., WILLIAM H. GODSICK, M.D., AND BENJAMIN SEGAL, M.D., NEW YORK, N. Y.

(From the Department of Obstetrics and Gynecology, Lincoln Hospital)

TO INTERRUPT pregnancy, the experienced abortionist usually resorts to the definitive procedure of dilatation and curettage or, in more advanced gestation, to simple dilatation and packing of the cervix. The less competent abortionist, or the patient herself, for that matter, may use a variety of other measures, some reasonably likely to succeed and others entirely useless.

The latter category includes, for instance, the insertion of potassium permanganate tablets in the vagina. In the former category, a popular method is the passage of a rigid or semirigid object through the cervix past the internal os for a variable period of time, with the intention of partially dilating the cervix, partially separating the conceptus or provoking contractions, and ultimately causing complete expulsion of the unwanted pregnancy. An accident that may occasionally result from this procedure is the loss of the aborting object within the pelvis or higher in the abdomen.

This study is concerned primarily with nonmetallic objects retained in the pelvis after recently attempted abortion, with special reference to urethral catheters. It is based on seven patients observed and operated on at Lincoln Hospital from 1947 to 1953; in six patients, a urethral catheter was removed at laparotomy, and, in one, a glass cocktail stirrer (Figs. 1*A* and 1*B*). In addition, the available recent literature on the subject has been reviewed. Details concerning our patients are presented in the following case reports, and pertinent features are summarized in Table I.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

TABLE I. SUMMARIZED DATA OF PATIENTS WITH FOREIGN

CASE	WEEKS OF AMENORRHEA AT TIME OF INSERTION OF FOREIGN BODY	DAYS FROM INSERTION OF FOREIGN BODY TO ADMISSION TO HOSPITAL	HISTORY OF INSERTION OF FOREIGN BODY WHEN ADMITTED	DAYS FROM ADMISSION TO HOSPITAL TO X-RAY EXAMINATION	DEMONSTRATION OF FOREIGN BODY BY X-RAY EXAMINATION	PALPATION OF FOREIGN BODY ON PELVIC EXAMINATION	DAYS FROM ADMISSION TO HOSPITAL TO LAPAROTOMY	TYPE OF FOREIGN BODY FOUND AT LAPAROTOMY
1. G. H.	20	3	Yes	3	Yes	No	3	16F. rubber catheter
2. A. M.	10	5	No	5	Yes	No	5	14F. rubber catheter
3. G. G.	13	3	Yes	<1	Yes	Yes	<1	14F. rubber catheter
4. H. S.	9	3	Yes	1 4	No Yes (column of air in radiolucent catheter)	No	7	14F. woven silk catheter
5. S. T.	12	1	Yes	1	No (faint shadow on review)	Yes	1	12F. woven silk catheter
6. C. T.	7	26	Yes	<1 2 4	No	Yes	4	12F. woven silk catheter
7. T. W.	5	1	Yes	<1	Yes	No	1	Glass cocktail stirrer

Case Reports

CASE 1.—G. H., a 21-year-old para ii, was admitted on Aug. 30, 1947, three days after she had inserted a rubber catheter into the vagina to induce abortion. She stated that the catheter "disappeared inside and did not come out." Shortly afterward, she began to bleed moderately, and then developed chills, fever, and lower abdominal pain. Her last menstrual period had been March 29, 1947. She thought she was approximately five months pregnant when she inserted the catheter. She gave no history of passing a fetus or recognizable tissue.

The patient appeared acutely ill with a temperature of 103.4° F. There was right lower quadrant rebound tenderness and moderate right costovertebral angle tenderness. The cervix was soft, and admitted one finger, and a foul, seropurulent watery discharge drained from it. The uterus was retroverted and tender, and seemed enlarged to the size of an eight weeks' pregnancy. The right fornix was markedly tender, but no definite mass was palpable.

BODIES LOST IN THE PELVIS DURING ATTEMPTED ABORTION

OPERATIVE FINDINGS			MORBIDITY			
LOCATION OF FOREIGN BODY	SITE OF PERFORATION	OPERATIVE PROCEDURES	HIGHEST PREOPERATIVE TEMPERATURE	HIGHEST POSTOPERATIVE TEMPERATURE	DAYS FROM OPERATION TO DISCHARGE FROM HOSPITAL	OUTCOME OF THE PREGNANCY
Partially enveloped by omentum	Uterus, fundus near right cornu	Removal of foreign body, suture of uterine perforation	103.4° F.	103.0° F.	26	Not pregnant
In localized abscess walled off by omentum and uterus	Uterus, anterior wall	Evacuation of abscess, removal of foreign body, drainage	103.8° F.	103.2° F.	21	Not stated (probably complete abortion prior to admission)
Free in peritoneal cavity	Uterus, fundus	Removal of foreign body, suture of uterine perforation, drainage	100.0° F.	100.2° F.	10	Incomplete abortion (subsequent curettage)
In canal created by omentum, cecum, ileum, appendix, and uterus	Uterus, low right posterolateral aspect	Lysis of adhesions, removal of foreign body, appendectomy, drainage	99.0° F.	100.0° F.	12	Complete abortion
Free in peritoneal cavity	Posterior fornix and cul-de-sac	Removal of foreign body, drainage	100.0° F.	100.2° F.	21	Pregnant when discharged (delivery of premature stillborn twins, four months later)
Partially retroperitoneal, partially intraperitoneal in localized abscess walled off by bowel and uterus	Posterior fornix and posterior visceral peritoneum	Lysis of adhesions, evacuation of abscess, removal of foreign body	101.4° F.	100.4° F.	11	Complete abortion
Free in peritoneal cavity	Uterus, fundus	Removal of foreign body	100.0° F.	100.0° F.	9	Not stated (probably not pregnant)

The sedimentation rate was 100 mm. per minute and the urine contained numerous white blood cells with clumps. X-ray examination of the abdomen three days after admission showed a catheter curled up in the right midportion of the abdomen.

The same day, on Sept. 2, 1947, at laparotomy, a 16F. brown, hard rubber catheter was found, with omentum wrapped partly about it, and was removed. The uterus was the size of a seven weeks' pregnancy and did not appear pregnant. On the fundus near the right cornu, a 5 mm. perforation was repaired, and the abdomen was closed without drainage.

Postoperatively, the patient was treated with penicillin, sulfadiazine, infusions, and blood transfusions. She had a moderately elevated temperature which gradually subsided before her discharge on Sept. 28, 1947, four weeks after admission.

Comment.—The delay of three days before x-ray study was due to total disbelief of the patient's history or to the unwarranted assumption that the catheter had dropped out of the vagina without her knowledge. Since the catheter was radiopaque, the diagnosis of retained foreign body was immediately apparent, and laparotomy was, of course, indicated.

As events proved, the patient had not been pregnant at all, and had attempted abortion in the mistaken belief that she was. Envelopment of the foreign body by the omentum is a common occurrence, exemplifying the defense role of this tissue. The uterine perforation —small, round, and smooth—was typical of those made by semirigid catheters, i.e., minimal destruction of tissue.

CASE 2.—A. M., a Spanish-speaking 20-year-old para i, was admitted on Sept. 10, 1947, with a history obtained through an interpreter of having slipped in the bathtub five days prior to admission. Immediately afterward she had a short bout of bleeding followed by fever, chills, watery stools, and severe right lower quadrant pain. Her last menstrual period was June 25, 1947; she was considered to be about two and one-half months pregnant at the time of admission.

The patient appeared acutely ill with a temperature of 103.8° F. There were rebound tenderness and a sense of increased resistance in the right lower quadrant. The cervix was soft and closed. There was no vaginal bleeding. The uterus was nontender, soft, and enlarged to eight weeks' size. A small, soft, very tender mass could be palpated in the right adnexal region. The sedimentation rate was 100 mm. per minute, a catheterized urine specimen contained white blood cells, and the white blood count was 14,000, with normal differential count.

The diagnoses entertained were parametritis and pyelitis, and the patient was treated with penicillin, sulfadiazine, and intravenous infusions. Symptoms continued, as well as fever ranging from 101° to 103° F. After several days of observations, a vague indistinct mass could be palpated on the right side of the abdomen. The tentative diagnosis at this time was cholecystitis with cholelithiasis. X-ray examination of the abdomen on Sept. 15, 1947, showed a catheter on the right side of the abdomen. When the patient was confronted with this information, she admitted having attempted abortion by inserting a catheter five days prior to admission.

At laparotomy on Sept. 15, 1947, a localized abscess, walled off by omentum, was found to the right of a slightly enlarged uterus. From the abscess cavity, a 14F. red, hard rubber catheter was removed, and 3 ounces of foul-smelling pus was evacuated, from which coliform bacillus, gamma streptococcus, and *Staphylococcus albus* were cultured. A small perforation on the anterior wall of the uterus had sealed over and required no further attention. Penrose drains were placed in the abscess cavity and the right lumbar gutter.

The patient continued to run a spiking temperature for about one week after operation, when right lower lobe pneumonitis was discovered. This subsequently cleared satisfactorily, and she was discharged on Oct. 1, 1947, three weeks after admission. She was seen at follow-up examination in 1950, when she informed us that she had had a cesarean section at another hospital in July, 1949.

Comment.—This was the only patient in our series who did not give a history of instrumentation on admission, possibly because of the language difficulty. Since the diagnosis was obscure, the abdomen was x-rayed prior to further radiologic investigation. Fortunately, the catheter was demonstrated by this simple procedure, and the diagnosis was apparent.

Not only had there been a five-day delay on her part before seeking medical attention, but the absence of a reliable history caused a further delay of five days before laparotomy. Her preoperative and postoperative morbidity would undoubtedly have been less if laparotomy could have been done sooner. As in the previous case, the omentum aided in localizing the process. The small perforation of the uterus caused by the catheter was already sealed over and hence did not require suturing. In all probability she had aborted prior to admission.

CASE 3.—G. G., a 30-year-old gravida iii, para 0, was admitted on April 16, 1951, with a history of having inserted a catheter to induce abortion three days prior to admission. The catheter slipped upward and could not be withdrawn. Her last menstrual period had

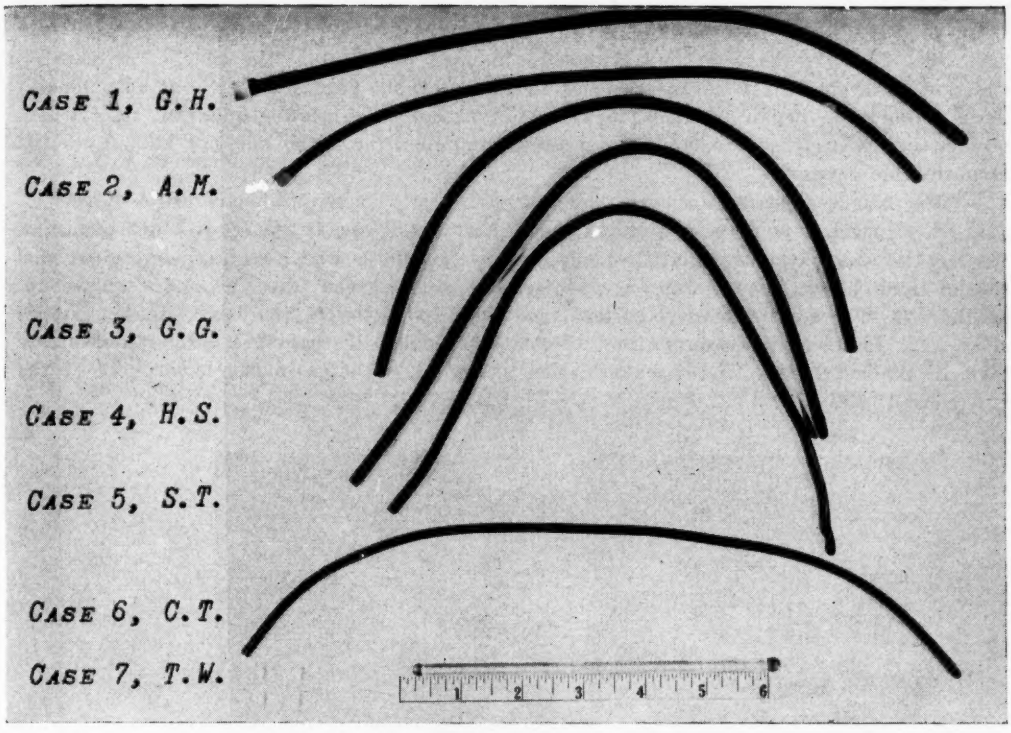


Fig. 1A.—Photograph of foreign bodies removed at laparotomy from 7 patients. The upper 3 catheters are of rubber, and the lower 3 catheters are of woven silk. The lowest object (near the ruler) is a glass cocktail stirrer.

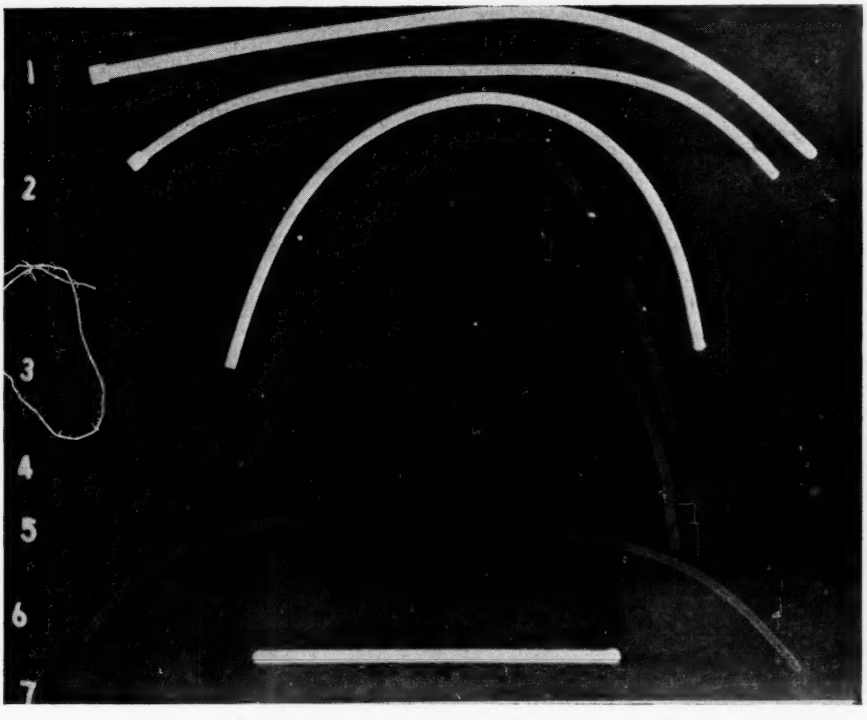


Fig. 1B.—X-ray of foreign bodies removed at laparotomy from 7 patients. Note the marked difference in radiopacity between the 3 upper catheters (rubber) and the 3 lower catheters (woven silk). The glass cocktail stirrer is of approximately the same order of radiopacity as the rubber catheters.

been Jan. 7, 1951; she was more than three months pregnant at the time of attempting abortion. The day after the insertion of the catheter, she passed a fetus but no placental tissue. She then began to experience right flank and right lower quadrant pain which became increasingly severe, and had mild vaginal bleeding. She had not had any chills or noticeable fever.

The patient appeared uncomfortable but not acutely ill, with a temperature of 100° F. There were marked tenderness, rebound tenderness, and spasm in the right lower quadrant. The cervix was patulous, admitting one finger, and there was a sanguineopurulent discharge from the os. The uterus was soft, tender, and enlarged to the size of a ten weeks' pregnancy. There were tenderness and some fullness in the right adnexal region but no mass. By rectovaginal examination, the catheter could be palpated lying transversely high in the cul-de-sac. X-ray examination showed a catheter in the lower half of the abdomen (Fig. 2).

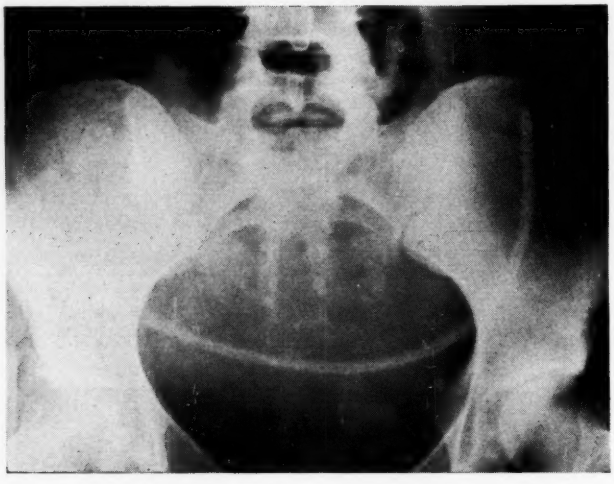


Fig. 2.—X-ray of abdomen of patient G. G. (Case 3), showing a rubber catheter in the lower half of the abdomen. The shadow outline has been heightened by "retouching" to compensate for loss of detail during photographic reproduction.

Laparotomy was performed on the day of admission. A 14F. red, hard rubber catheter was found lying free in the peritoneal cavity and extending down to the cul-de-sac. The object was removed, and a small perforation in the fundus of the uterus was repaired. The peritoneal cavity contained a small amount of seropurulent fluid, from which *Aerobacter aerogenes* and nonhemolytic streptococcus were cultured. The abdomen was closed with drainage. Penicillin and streptomycin were administered postoperatively. The course was entirely uneventful, the temperature never rising above 100° F. The patient was discharged on April 25, 1951, ten days after admission.

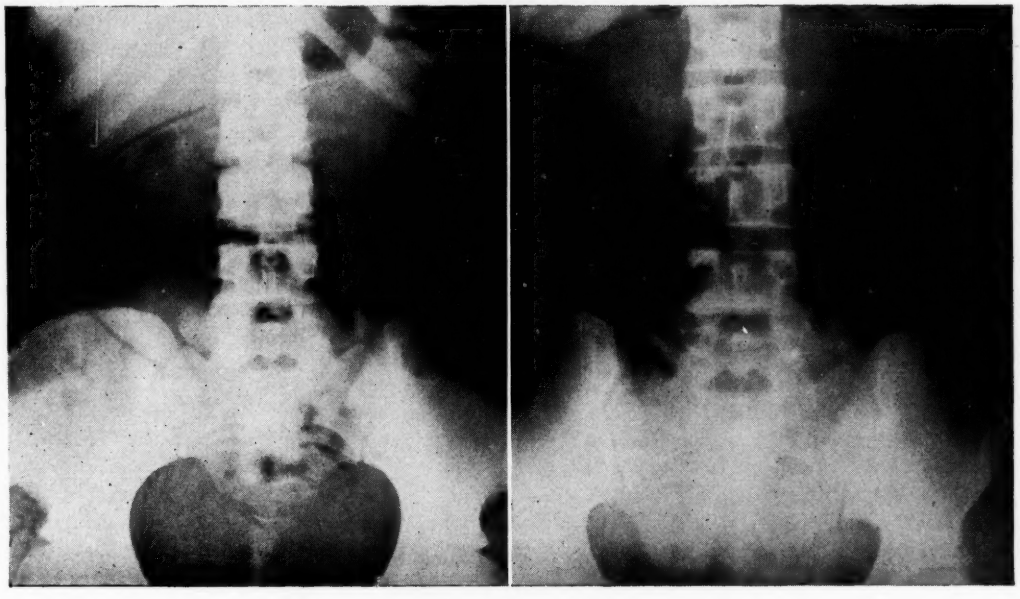
She was readmitted one month later on May 24, 1951, because of vaginal bleeding and passage of tissue. With sponge stick and dull curette, many fragments of placental tissue were removed. She did well and was discharged four days later.

Comment.—In this case, not only the history but also the palpatory findings indicated the diagnosis, so that a radiograph of the abdomen was taken shortly after admission. Upon the radiologic demonstration of a catheter in the pelvis, laparotomy was done immediately. Her preoperative morbidity was minimal and the postoperative course benign.

No attempt was made before operation to curette the uterus for removal of the retained secundines because of the suspected uterine perforation. One month later, when the patient passed tissue spontaneously, the abortion was carefully completed in the knowledge that the perforation had certainly healed by that time.

In this instance, as opposed to the two previous cases, the catheter lay free in the pelvis without envelopment by the omentum. Even though laparotomy was done within four days of the insertion of the catheter, early peritonitis was present, as evidenced by the small amount of seropurulent fluid in the pelvis. Although drainage was instituted at the time of operation, in retrospect this was probably not necessary.

CASE 4.—H. S., a 26-year-old para iii, was admitted on Nov. 3, 1952, with a history of having inserted a catheter three days prior to admission. Since then, she had been "unable to find it." Several hours after the manipulation, she began to have crampy lower abdominal pains and mild vaginal bleeding, followed by vomiting, chilly sensation, and mild fever. Her last menstrual period had been Sept. 1, 1952; she was approximately two months pregnant when the catheter was inserted.



A. *B.*

Fig. 3.—*A*, X-ray of abdomen (recumbent position) of patient H. S. (Case 4), showing a curvilinear shadow of decreased density in the upper right side of the abdomen, representing a column of air within a radiolucent catheter (woven silk).

B, X-ray of the same patient, taken in the upright position, showing the same structure lower in the abdomen.

The shadow outlines have been heightened by "retouching" to compensate for loss of detail during photographic reproduction.

She appeared in pain but not acutely ill. The temperature was 100° F. The abdomen was slightly distended, with some voluntary rigidity. There was tenderness to deep palpation, especially on the right, but no rebound tenderness. The cervix was slightly patulous, with yellow discharge from the os, but no bleeding. The uterus was slightly tender, boggy, and enlarged to the size of a ten weeks' pregnancy. There was no adnexal tenderness or mass. The sedimentation rate was 130 mm. per hour.

X-ray examination of the abdomen on Nov. 4, 1952, was first reported negative. Because of the history, these films were reviewed and other films were taken on Nov. 7, 1952. It was then concluded that there was a curvilinear formation of decreased density, 20 cm. long, in the right side of the abdomen (Fig. 3, *A* and *B*). This formation was judged to represent a radiolucent catheter containing a column of air or other gas.

The patient was treated with penicillin, streptomycin, and intravenous infusions; the abdomen remained soft, there was no fever, and the general condition was good. Laparotomy was done on Nov. 10, 1952, one week after admission. After separation of adhe-

sions of small bowel to the uterus, a 14F. woven silk catheter was seen in the right lumbar gutter. It lay in a sort of sinus created by omentum, cecum, ileum, appendix, and the right side of the uterus, extending down to a small, sealed-over perforation low on the right posterolateral aspect of the uterus. The catheter was removed; it was not considered necessary to suture the perforation. Appendectomy was performed because of the mildly inflamed appearance of the appendix, and the abdomen was closed with drainage. The pathologic report was mild diffuse appendicitis and periappendicitis.

The next day the patient expelled fetus and placenta. The subsequent course was uneventful, and she was discharged on Nov. 22, 1952, twelve days after operation.

Comment.—In this case, the catheter itself was radiolucent, but the diagnosis was made by the thin column of gas corresponding to the shape and caliber of a catheter. The gas within the catheter could have been entrapped air or gas produced by a gas-forming bacillus such as *B. welchii.* Unfortunately, cultures were not taken at operation, so that the infecting organism was not identified. The general appearance of the patient did not suggest a *B. welchii* infection.

The process was localized by omentum and other organs. As is frequently the case, the small perforation was sealed over, so that suture was not required. Appendectomy is, of course, neither customary nor advisable during laparotomy for removal of a foreign body. In this case, however, appendectomy was done because of the inflamed appearance of the appendix, due undoubtedly to its close proximity to the inflammatory process.

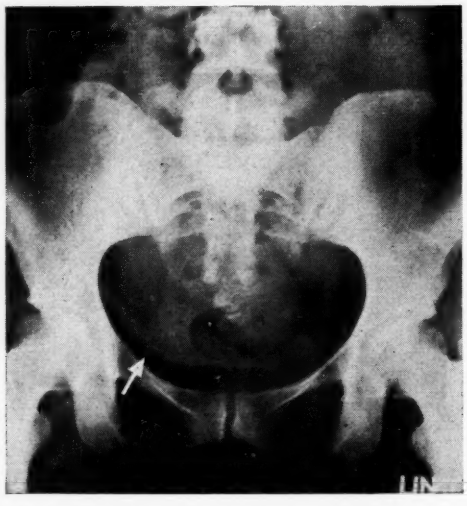


Fig. 4.—X-ray of abdomen of patient S. T. (Case 5), which was originally reported as negative. On review of the film in preparation for this report, however, a faint outline of a portion of the catheter (woven silk) could be seen in the lower right side of the pelvis. The shadow outline has been heightened by "retouching" to compensate for loss of detail during photographic reproduction.

CASE 5.—S. T., a 31-year-old para viii, was admitted on July 21, 1953, with a history of having introduced a rubber catheter into the vagina the night before, in order to induce abortion. The catheter "remained inside and was still inside." Shortly after the insertion of the catheter, she experienced lower abdominal pain and slight vaginal bleeding. The last menstrual period had been April 18, 1953; she was about three months pregnant at the time.

She did not appear acutely ill or in any great pain. The temperature was 99.8° F. The abdomen was soft and flat, with mild tenderness in the right lower quadrant. The cervix was closed without bleeding. The uterus was soft, symmetrical, nontender, and enlarged to twelve weeks' size. A tender mass of indefinite size, suggestive of a catheter,

was palpated in the cul-de-sac. X-ray examination of the abdomen on July 22, 1953, was judged to show no evidence of an opaque foreign body. There was marked gas distention of the intestines in the upper part of the abdomen.

Laparotomy was performed on July 22, 1953. A 12F. woven silk catheter was found lying free in the peritoneal cavity in the lower pelvis and was removed. A small perforation in the cul-de-sac, about 5 mm. in diameter, had sealed over with filmy adhesions. There were no bleeding and no peritoneal fluid or collection. The uterus was pregnant and twelve weeks' size, without perforation, and intact. The abdomen was closed with drainage. The patient was treated postoperatively with penicillin and streptomycin. The postoperative course was uneventful and the patient was discharged on Aug. 12, 1953, 21 days after operation. She was readmitted on Nov. 18, 1953, about four months after operation, because of abdominal pain. Although she was seven months pregnant, the abdomen was greatly distended and the fundus reached to the xyphoid process. No fetal heart sounds could be heard. Two days later she went into labor and after seven hours was delivered of premature macerated twins. She was discharged in good condition on the fifth postpartum day.

Comment.—In the absence of x-ray findings indicative of a foreign body, laparotomy was decided on because of the history and the mass suggestive of a catheter palpated in the cul-de-sac. The radiograph was originally reported as negative. When the films were reviewed in preparation for this report, however, a faint outline of a portion of the catheter could be made out in the lower pelvis (Fig. 4).

In contrast to the preceding cases, the catheter had penetrated into the peritoneal cavity by perforating the posterior fornix and cul-de-sac rather than the uterus. Possibly the diagnosis of mode of entry might have been made if the vaginal fornices had been examined more thoroughly.

CASE 6.—C. T., a 35-year-old para iv, was admitted on Aug. 31, 1953. Her last menstrual period had been about June 15, 1953. On Aug. 5, 1953, at some seven weeks' amenorrhea, she had inserted a catheter to induce abortion. The catheter "disappeared" and the patient "did not see it any more." She spotted and bled mildly for three or four days but did not experience any abdominal pain. She then consulted her physician, who considered this to be an inevitable abortion and performed dilatation and curettage on Aug. 17, 1953. The tissue obtained (amount not specified) was reported as "chorionic villi." About five days after curettage, she began to experience intermittent sharp lower midabdominal, right lower quadrant, and low back pain, which persisted.

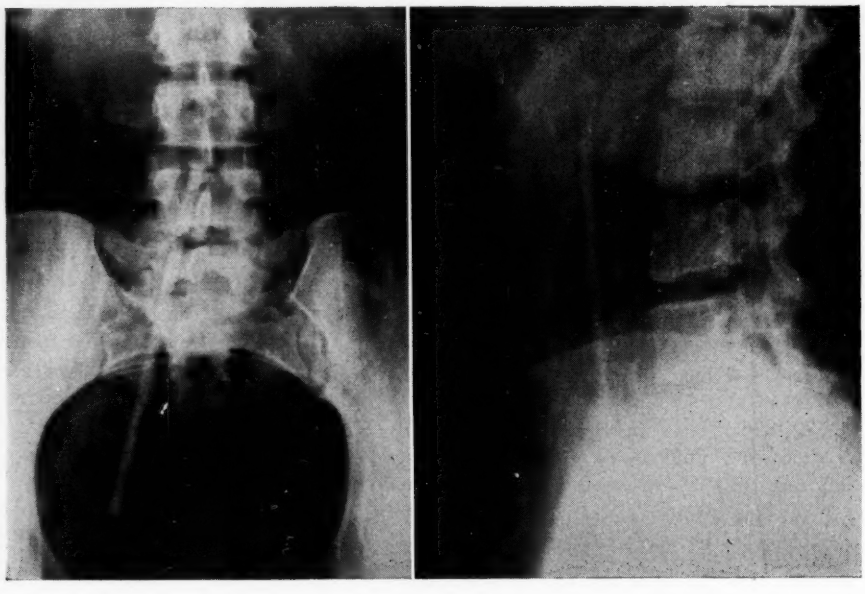
She did not appear acutely ill but was in moderately severe discomfort. The temperature was 100° F. and the sedimentation rate was 130 mm. per minute. The abdomen was soft and somewhat distended, with mild tenderness in the upper portion of the right lower quadrant. The cervix was slightly patulous, and there was a small amount of sanguineous discharge from the os. The uterus was soft, nontender, and enlarged to three months' size. There was no adnexal tenderness. Behind the cervix, and seeming to lie transversely in the cul-de-sac was a thin, firm, elongated structure of the size and consistency of a catheter. Three successive x-ray examinations with varied views did not reveal any opaque foreign body in the abdomen or pelvis.

At subsequent pelvic examinations, others as well as the original observer could not palpate the foreign body, which apparently had been displaced upward during the initial examination. Penicillin and streptomycin therapy was instituted and, in view of the uncertainty of the diagnosis, it was decided to observe the patient further. Her temperature rose during the next few days to 101.4° F., the abdominal tenderness increased, and rebound tenderness and voluntary rigidity appeared. On repeated questioning, the patient affirmed her conviction that the inserted catheter "did not fall out and was still inside."

In view of the progression of the abdominal signs and reaffirmation of the history, laparotomy was done on Sept. 4, 1953, four days after admission and about one month after insertion of the catheter. The uterus was about three months pregnant, presented

no perforation, and was adherent posteriorly at the midportion for an area of about 2 inches in diameter. Large bowel was adherent to the fundus of the uterus by dense fibrinous adhesions. When these were freed, about 60 c.c. of pus was liberated, from which *B. coli* was cultured. The uterus was then gently separated by finger dissection from its posterior adherence. At this point, a catheter tip was felt barely protruding through a rent in the posterior visceral peritoneum, and a 12F. silk woven catheter was then withdrawn. It had evidently been pushed through the posterior fornix, had traveled upward retroperitoneally for a short distance, and had then perforated the posterior visceral peritoneum, where a localized abscess had formed, walled off by large intestine, posterior surface of the uterus and posterior parietal peritoneum. The abdomen was closed without drainage.

Postoperatively, penicillin and streptomycin were continued and three transfusions were administered. The day after operation, the patient passed the fetus and placenta. The temperature did not rise above 100° F., and the course was uneventful except for transitory mild distention. She was discharged on Sept. 15, 1953, eleven days after operation.



A. *B.*

Fig. 5.—*A*, X-ray of the abdomen of patient T. W. (Case 7) showing a glass cocktail stirrer.

B, Lateral view of the same patient.

Comment.—This very interesting case illustrates the difficulty of diagnosis when the catheter does not show up on the radiograph. The history of insertion of a catheter was quite definite. What was less readily understandable was the continuation of the pregnancy despite a curettage reported to be productive of tissue diagnosed microscopically as chorionic villi. Consequently, some observers doubted the validity of the history entirely. In view of the progression of signs of peritoneal irritation, however, and the patient's insistence that she had indeed inserted a catheter which had remained inside, laparotomy was finally decided on.

As in the previous case, the catheter had perforated the posterior fornix without injuring the uterus. In contrast, however, its pathway into the peritoneal cavity was less direct, and major infection was present, as evidenced by the localized abscess. Despite

the intraperitoneal abscess, the postoperative course was entirely uneventful, due, surely, to antibiotic therapy. It is interesting to note that drainage was not instituted in this case.

CASE 7.—T. W., a 25-year-old para i, was admitted on June 11, 1952, having inserted a glass cocktail stirrer into the vagina the evening before in order to induce abortion. In the morning prior to being admitted she "could not find the glass rod." She had slight vaginal bleeding and mild lower abdominal pain after the manipulation. Her last menstrual period had been May 5, 1952, and she was about one week overdue.

She did not appear acutely ill. The temperature was 99.8° F. The abdomen was soft, flat, and nontender. The cervix was patulous and there was slight bleeding from the os. The uterus was in second-degree retroversion, nontender, enlarged to seven to eight weeks' size, and apparently firm. There was mild tenderness in the left adnexal region but no mass. X-ray of the abdomen on the day of admission showed a straight longitudinal foreign body in the lower half of the abdomen anterior to the lumbar vertebrae (Fig. 5, *A* and *B*). The urine was negative, and the hemoglobin was 14 Gm.

At laparotomy on June 12, 1952, a 6 inch, faintly green-colored glass rod with rounded ends was removed from the peritoneal cavity, which contained no blood or fluid. The uterus was enlarged to seven weeks' size. At midfundus, a 5 mm. perforation had sealed over and repair was not considered necessary. The postoperative course was uneventful on penicillin therapy, the temperature never rising above 100° F. The patient was discharged on June 20, 1952, nine days after operation. She was seen in the follow-up clinic on Aug. 13, 1953. She had had normal periods since the operation and gave no history of passing tissue. The pelvic examination was entirely negative.

Comment.—Although, in this series, urethral catheters were the objects by far the most frequently used to induce abortion, this patient employed a glass stirrer because, as she informed us, "she had one handy." In view of the history and the x-ray findings, the diagnosis was readily made. As with the rubber catheters, the uterine perforation made by the glass stirrer was small and, in this instance, did not require repair.

Although the possibility of pregnancy with early abortion could not be ruled out, it was felt that, in all probability, this patient had not been pregnant.

Types of Foreign Bodies

The extensive injuries produced by inept and overly persistent abortionists are a matter of common knowledge. These may result from the use of sharp instruments, such as curette or sound. It is the grasping instruments, however, such as ovum forceps or dressing forceps, that usually produce the most serious damage—particularly large, jagged, or multiple openings in the uterus, avulsion of omentum, laceration of intestine, stripping of mesentery, and herniation of bowel through the uterine rent into and even beyond the vagina.[1] The responsible instruments are withdrawn immediately after the procedure, and the clinical picture is that of septic abortion with severe or overwhelming peritonitis. This condition is beyond the scope of the present report.

When foreign bodies are left in the pelvis after attempted abortion, the initial injury is usually rather minor, partly because of the very nature of the object but mainly because of the manner in which it is used. Since the purpose is not to complete an abortion but rather to start it, the object is usually introduced but once. There is, in other words, no repetitive trauma, and the extent of the trauma is necessarily limited by the size, length, rigidity, and general facility of handling of the particular object. Moreover, since these objects are frequently introduced by the patients themselves, pain and fear usually do not permit the extensive manipulation that is more likely to produce serious injury.

What may these objects be? They are conveniently classified into two categories, metallic and nonmetallic. Metallic foreign bodies include hatpin,

hairpin, bobby pin, knitting needle, crochet hook, metal syringe tip, umbrella rib, metal catheter, as well as pieces of curette accidentally broken off. Nonmetallic foreign bodies include celluloid or plastic bobby pin, rubber or bone penholder, rubber enema tip, earpiece of shell-rim eyeglasses, pencil, pieces of wood (particularly slippery elm bark), glass catheter, stirring rod and drinking tube, and urethral bougies and catheters.

This list, surely not exhaustive, illustrates the great diversity of foreign bodies, limited only by their availability and by the patient's imagination as well as, perhaps, her state of desperation. Yet certain trends are apparent. Metallic objects have become relatively uncommon in recent years, possibly because of a realization of their greater potential danger. Slippery elm bark, no longer popular in this country, is apparently still well regarded in England where its use recently called forth an anguished protest: "Why the bark of this noble tree should be so popular is difficult to understand."[2] An ingenious method promulgated by midwives in northern France consisted in the cervical insertion of medicated urethral bougies or crayons, made of solidified glycerine, and originally intended for the local treatment of male urethritis. The advantages of this procedure were considerable: being semirigid, the bougie could easily be inserted; it usually provoked uterine contractions and, ultimately, abortion; it was antiseptic; and it could be left in place whence it finally disappeared by dissolution, without leaving incriminating evidence.[3]

Both in this country and abroad, urethral bougies and catheters have long enjoyed a considerable vogue, and catheters, in particular, have become even more popular within recent years. In Tcherlok's[4] collected series up to 1929, there were 41 cases of foreign bodies in the peritoneal cavity; of 30 cases in which mention was made of the nature of the object, 21 were urethral bougies or catheters. In Crossen and Crossen's[5] remarkable book, "Foreign Bodies Left in the Abdomen," a section is devoted to articles found in the peritoneal cavity after abortion attempts. In a total of 33 cases collected up to 1938, there were seven urethral bougies, six urethral catheters, ten metallic objects, and ten miscellaneous nonmetallic objects. In our survey of the more recent American and available European literature, we found a total of 23 reported cases of foreign bodies in the pelvis (peritoneal cavity and retroperitoneal spaces) after abortion attempts. Of these, there were one urethral bougie, twelve urethral catheters, one metallic object, and nine miscellaneous nonmetallic objects.[6-28] In our own series of 7 cases, there were six urethral catheters and one glass object.

The popularity of the urethral catheter as a means of inducing abortion is due to: (1) its ready availability without undue difficulty or opprobrium because of its primary function; (2) its semirigid consistency and somewhat blunted tip, affording sufficient stiffness and penetration for the intended purpose without the obvious danger inherent in sharp metallic objects; (3) its length, facilitating handling; and (4) its easy sterilizability, should that be felt necessary.

Modes of Entry of and Bodily Reactions to Foreign Bodies

Most often, the abortifacient object is introduced through the cervix, perforates the uterus, usually at the fundus or anterior wall, and lodges in the peritoneal cavity, without further visceral injury. There it may lie free, usually in the lower portion, as in Cases 3 and 7. Frequently the omentum tends to envelop the foreign body, either by itself, as in Case 1, or with the aid of the pelvic organs, as in Case 4.

If the foreign body is relatively clean, if the perforation causes minimal intraperitoneal bleeding, and if operation is performed soon after the accident, peritoneal reaction is usually minimal. Generalized peritonitis of a serious

degree may occur but is not common, probably because of: (1) the frequency with which patients, fearful of the consequences of the retained foreign body, seek medical attention early; (2) the protective role of the omentum; (3) the relatively minor degree of injury to the uterus; and (4) the infrequency of bowel injury.

The inflammatory process, if minor, may subside, so that the foreign body remains encapsulated indefinitely as a sort of enclave within the host, causing few if any symptoms; or else a localized abscess may form, as in Case 2, with signs and symptoms of infection and peritoneal irritation.

Occasionally, the object may perforate the upper portion of the cervix or lower portion of the uterus, passing retroperitoneally into the parametrium and broad ligament. Sometimes the posterior vaginal fornix is perforated, whence the object may enter the peritoneal cavity directly through the cul-de-sac, as in Case 5; or indirectly after first traversing the retroperitoneal space, as in Case 6; or it may remain entirely retroperitoneal. In Dawson's[18] patient, the foreign body perforated the left vaginal fornix, and passed under the right common iliac vessels, to lodge finally between the inferior vena cava and the vertebral bodies; uneventful recovery followed removal of the foreign body. In Codazzi's[14] patient, the foreign body, after passing through the cul-de-sac, perforated the sigmoid, producing a fecal abscess; this patient died after operation.

Unusual places of lodgement of foreign bodies are the broad ligament,[13] the Fallopian tube,[7, 28] the ischiorectal fossa,[15] and the lumbar region.[22] Probably the most bizarre case in the literature is that of Bláha.[8] The catheter had perforated the cervix 2 cm. above the os, passed into the right parametrium and through the uterine plexus into the right hypogastric vein and then embolized; at autopsy, it was found extending from the inferior vena cava just above the diaphragm, through the right heart into the superior vena cava, and finally to the left common jugular.

Not all foreign bodies inserted into the uterus necessarily perforate it. They may be expelled along with the products of conception or may be tolerated by the uterus and the growing pregnancy for a variable period of time. Among reported nonperforating intrauterine foreign bodies inserted for abortion are metal hairpin, metal bobby pin, brass wire, penholder, laminaria, urethral catheter and bougie, assorted pins, feathers, stalks of diverse plants, and pieces of old shoe leather.[4, 29-34]

On occasion, the foreign body finds its way into the bladder, either indirectly via a uterovesical fistula created by it or, more commonly, directly through the urethra because of the patient's erroneous notions of anatomy. Common objects are metal hairpin, slippery elm bark, and urethral catheter.[2, 35, 36] Attention is usually directed to this organ by symptoms of cystitis.

What happens to an intraperitoneal foreign body months or years after subsidence of the initial inflammatory reaction? Following paths of least resistance, it may migrate to the abdominal wall, presenting as a fluctuant swelling due to aseptic abscess, as in the case of Ross and McLellan.[25] Or, propelled by peristaltic movements, it may finally lodge near a loop of bowel and slowly perforate it, causing localized peritonitis, as in the cases of Pamperi[23] and of Prevedi.[16] Or it may call attention to its presence when a hard, fixed tumor is formed by the foreign body bound to adjacent organs by adhesions and fibrous tissue; or remain dormant for as long as twenty-five years, as in the cases cited by Crossen and Crossen,[5] only to be discovered during x-ray studies for investigation of vague abdominal symptoms and obscure complaints.

Since the history of previous insertion of a foreign body is usually forgotten by patients after a lapse of years, these belated cases are difficult to

diagnose, unless x-rays demonstrate the foreign body. The special problems posed by such "chronic" foreign bodies are not under consideration in this report, which deals primarily with the diagnosis and management of recently inserted foreign bodies.

Outcome of Pregnancy

When a foreign body is inserted into the pregnant uterus without perforating it, it generally expels the pregnancy along with the object. However, the tolerance of the uterus to foreign bodies is at times remarkable. Thus, pregnancy has occurred and continued to term in the presence of a pre-existing intrauterine foreign body, e.g., a piece of cotton remaining after packing for hemorrhage following a previous delivery,[37] and a gauze sponge inadvertently left in the uterus at a previous cesarean section.[38] In the case reported by Kimbrough and Tompkins,[39] a pre-existing Gräfenberg ring was removed at two months' gestation, the pregnancy continuing to term. In Freedman's[40] case, a gold wedding ring (previously inserted as a contraceptive measure) remained in the uterus with the pregnancy until four weeks before term, when it was passed spontaneously, the pregnancy continuing normally. In Ellison's[34] case, a catheter, inserted into the uterus at about five months' gestation, remained there until it was passed spontaneously six weeks before term; the pregnancy continued normally. Rarely, the foreign body may cause dystocia, as in the case of a wooden spool reported by Nuñez[41]; after its removal, successful delivery was effected.

On occasion, the vitality of the ovum is affected so that it dies in several months. Thus, in Cashwell's[33] case, a metal bobby pin was inserted at six weeks' amenorrhea; a dead fetus of approximately four months' gestation was subsequently removed by hysterotomy; the foreign body was found between the placenta and the anterior uterine wall, at the center of the placental attachment.

When the uterus is perforated by the foreign body, abortion usually ensues. Thus, in our 3 cases of perforation of a pregnant uterus, abortion occurred definitely in 2 (Cases 3 and 4) and probably in one prior to admission (Case 2). Yet in the occasional case pregnancy may continue to term. Bateman[12] reported a case of uterine perforation by catheter at three months' gestation. The catheter was removed from the peritoneal cavity and adhesions of sigmoid to the perforation were not disturbed; the pregnancy continued to term. In the case of Cohen and Fleischer,[17] perforation occurred shortly after a missed period. One end of the catheter was free in the pelvis and the other end perforated the anterior surface of the uterus. The catheter was removed, the perforation was repaired and the pregnancy continued to term.

If the foreign body perforates the cul-de-sac without injuring the uterus, one might reasonably expect continuation of the pregnancy. Abortion occurred in both of our two cases, however (Cases 5 and 6). Two similar cases culled from the literature likewise terminated in abortion.[18, 26]

It is well to remember that not all women who insert or undergo insertion of foreign bodies to induce abortion are necessarily pregnant. In our series of 7 cases, one was definitely not pregnant (Case 1) and one was probably not pregnant (Case 7). In 23 cases from the literature, 5 patients were found not to be pregnant.[11, 20, 22, 24, 25] Insertion of foreign bodies may also occur in the presence of tubal pregnancy.

Diagnosis

Diagnosis is based on the history, the physical findings, the x-ray examination, and evaluation of the patient's course. Of these, the most important are

history and x-ray. In the absence of suitable history, diagnoses most frequently entertained are septic abortion, pyelitis, acute apendicitis, appendiceal abscess, and cholecystitis.

History.—Since the entire situation revolving about induced abortion is fraught with dissimulation, the history is generally considered unreliable. Yet, when a patient knows that a foreign body has been inserted and remains within, she is uneasy and fearful—realizing that this is *contra naturam*—and is more likely to tell the truth. Consequently, such a history should be accepted at face value; the unwarranted assumption should not be made that the foreign body must have passed out without the patient's knowledge. Every effort must be made to prove the patient's statement, and, of course, the major step in this direction is the flat film of the abdomen. All except one of our patients gave a history on admission of insertion of foreign body.

What if the x-ray does not show any foreign body, and there are no other findings to verify or at least lend substantial support to the history? Here, much depends on the acumen and astuteness of the physician in evaluating the patient's credibility. If a decison cannot be made, further observation of the patient's course may clarify the picture.

On the other hand, some patients do not give a proper history on admission, stating merely that there has been a fall or similar minor accident. If a foreign body is fortuitously discovered on a radiograph taken for other reasons, the patient usually admits to instrumentation when confronted by this evidence, as in Case 2. Rarely, admission is not forthcoming even then.

Physical Findings.—Infection is usually present, as evidenced by fever, tachycardia, elevated erythrocyte sedimentation rate, and leukocytosis. Peritoneal irritation or early peritonitis or localized intraperitoneal abscess is suggested by abdominal tenderness, rebound tenderness, and muscular spasticity. These findings are not characteristic, however, and occur also in septic abortion with parametritis and peritonitis, not associated with foreign body. Pelvic examination is also generally not particularly contributory, except when the foreign body is palpated, as in Cases 3, 5, and 6. Careful inspection of the vaginal fornices may demonstrate a perforation. Palpation of a tender adnexal mass is puzzling; it may simply represent an associated adnexitis or may indeed be part of the foreign body surrounded by exudate or omentum. With a good history and even without x-ray confirmation, such a finding may suffice to indicate laparotomy.

On occasion, when the diagnosis is in doubt, the progression of signs and symptoms of peritoneal irritation during a reasonable period of observation may help clarify the picture, as in Case 6.

X-ray Examination.—If all objects used to induce abortion were radiopaque, the problem would be greatly simplified. Metallic foreign bodies are, of course, easily demonstrable by x-ray examination. Nonmetallic foreign bodies, however, vary considerably in their opacity to x-ray. Clear glass is usually radiolucent, but glass objects to which some color has been imparted by admixture of even small amounts of metallic salts or oxides (e.g., of lead or iron) are radiopaque. As to urethral catheters, with which we are here especially concerned, the basic materials of which they are made—rubber, silk, and shellac, and various plastics—are radiolucent. In the course of manufacture, however, substances are added which may coincidentally produce radiopacity. Thus, iron oxide is added to impart a red color to rubber catheters, and cadmium selenide to vinyl plastic catheters. Stabilizers used in the processing of vinyl plastic include compounds of lead, barium, and tin. In the manufacture of woven silk catheters, extremely small quantities of cobalt, lead, or manganese are added as driers; frequently, the amounts are too small

to impart appreciable radiopacity. Most polyethylene tubing is radiolucent; however, barium sulfate is added when radiopaque tubing is desired. In our 3 cases of rubber catheters, all proved radiopaque. Our experience is borne out, in the main, by that of other authors. Vinyl plastic catheters are of the same order of radiopacity. Silk woven catheters are less uniformly radiopaque. Thus, in our 3 cases of silk woven catheters, one was radiolucent at repeated examinations; one was considered radiolucent at the original examination but, on subsequent careful review of the films, a faint outline of a portion of the catheter could be seen; and one was radiolucent but contained within it a column of air or other gas, which ultimately permitted the diagnosis. The differences in radiopacity of the foreign bodies removed from our patients are shown in Fig. 1*B*.

Usually, a radiopaque object will be readily apparent even on a poor x-ray film. Objects with relatively little radiopacity may easily be missed, however, unless great care is exercised in taking and interpreting the film. The entire abdomen and pelvis should be included. If the initial x-ray examination is negative, repeat x-ray studies are advisable, with variations in exposure, positioning, etc. And, above all, the reading of the film must be unhurried and detailed. Occasionally, when a history of insertion is lacking, a foreign body may be an accidental finding on x-ray films taken for other reasons.

In addition to demonstrating the presence of a foreign body, the radiograph shows its general location, thus facilitating its removal at operation. With the flat film of the abdomen, one can usually differentiate between an intraperitoneal foreign body and one retained within the uterus. In special cases, auxiliary procedures may be employed, such as x-ray examination of the abdomen with a metal sound within the uterus (if there is no viable pregnancy) or hysterography.[42, 43]

X-ray examination is, of course, indicated immediately whenever there is a history of foreign body retained in the pelvis. It is also advisable in all cases of suspected septic abortion where the response to customary therapeutic measures is unsatisfactory or the clinical course otherwise unusual.

In 6 of our patients who, on admission, gave a history of insertion of foreign body, the history was verified either by the x-ray findings or by the pelvic examination and the clinical course, or both. In the remaining patient, who did not give a history on admission, the diagnosis was made accidentally by the radiograph.

Management

The diagnosis of foreign body in the pelvis necessarily means its removal. Before proceeding to operation, it is necessary to determine the location of the object, if possible. A foreign body retained within the bladder betrays itself by symptoms of cystitis. Corroboration is obtainable by cystoscopic examination, and removal is effected through the urethra or, if that is not feasible, by cystotomy. Intrauterine foreign body is more difficult to locate. X-ray examination is helpful if the object is radiopaque. After cervical dilatation under anesthesia, it may be palpated by the finger, sound, or curette. Generally, removal of intrauterine foreign body is easily effected after cervical dilatation or incision.

In the case of the more common intraperitoneal foreign body, laparotomy is the procedure of choice. Colpotomy has been used on occasion, but this cannot generally be recommended because most foreign bodies are not palpable in the cul-de-sac, and, even if a foreign body were considered removable by this route, inspection for visceral injury could not be done.

If the foreign body is large, like a urethral catheter, it usually can be located without difficulty, as in our cases. If, however, it is small, a diligent and time-consuming search may be necessary, and even then may not prove rewarding. If the foreign body is not seen immediately, it should be sought in or near the omentum, in any areas where loops of bowel are matted together, and particularly in the right side of the abdomen, since foreign bodies are more often found there than on the left. If careful inspection of the peritoneal cavity does not disclose the foreign body, attention should be directed to the retroperitoneal spaces, particularly the broad ligaments. In Weisberg's[13] case, a catheter in the abdomen had been demonstrated by x-ray examination. At laparotomy, however, the catheter was not visible or palpable anywhere in the peritoneal cavity. The uterus did not present any perforation, but close inspection revealed a very small perforation of the broad ligament through which the tip of the catheter could be grasped and withdrawn.

If the uterine or cul-de-sac perforation is small, as is usually the case, spontaneous closure tends to occur early either by sealing over with fibrinous exudate, or by omental or bowel adhesion. Thus, in Stokes'[27] case, though the patient was operated upon five hours after perforation of the uterus by a pencil, omentum was already firmly adherent to the perforation. In such cases, the area need not be disturbed and suture is not required. If, however, the perforation has not closed, one or two sutures are in order.

Although intestinal or other major visceral injury is uncommon, it is important to rule it out by careful and thorough inspection. If such injury is found, repair is, of course, necessary. In none of our cases was any bowel injury found.

Should the abdomen be drained? Neither in our cases nor in those cited in the recent literature has there been a consistent policy in this regard. With antibiotic therapy, it seems that drainage is usually not necessary, even in the presence of localized abscess, as in Case 6.

In the usual case of uterine perforation, hysterectomy is definitely not indicated. It may be considered in the occasional case with generalized peritonitis.

Prognosis

The prognosis is usually good. Some patients barely appear ill; and those who do show clinical evidence of infection do not present the picture of overwhelming sepsis seen in patients with septic abortion associated with peritonitis. At laparotomy there is usually either no evident peritoneal reaction or early pelvic peritonitis or localized abscess. Generalized peritonitis is uncommon. In the occasional case of bowel injury, there is localized peritonitis at the site of perforation, which may become generalized.

Recovery is generally to be anticipated, the morbidity varying directly with the degree of infection, the extent and nature of visceral injury, and the time elapsed between insertion of the foreign body and operation. Antibiotic therapy also plays an important role in reducing morbidity.

The mortality rate has been relatively low even in the presulfonamide era. Thus, in 40 cases collected by Teherlok[4] prior to 1929, there were 3 deaths (8 per cent). In 33 cases collected by Crossen and Crossen[5] from the turn of the century to 1938, there were 2 deaths (6 per cent), both occurring after insertion of sharp metallic objects. In a review of 23 cases cited in the more recent literature, there were 2 deaths (9 per cent), one due to embolization of a catheter to the heart,[8] and one due to perforation of the sigmoid by a catheter with formation of fecal abscess.[14] In our series of 7 cases there were no fatalities.

Summary

On the basis of our experience with 7 cases of intraperitoneal foreign bodies, mainly urethral catheters, following abortion attempts, as well as a review of the recent literature on this subject, certain conclusions may be reached regarding diagnosis, management, and prognosis.

Diagnosis is based primarily on the history and radiographic findings, and secondarily on physical findings and course. Most often a reliable history of insertion of a foreign body is forthcoming and should immediately indicate x-ray examination. This is also advisable in all cases of suspected septic abortion with inadequate response to customary treatment.

The radiograph is extremely valuable in most cases because of the relative radiopacity of the objects now commonly employed, particularly urethral catheters. Some types of catheters, however, as well as other nonmetallic objects, are radiolucent. A negative x-ray examination should be checked by repeated study and the interpretation carefully reviewed, since some objects may be barely visible on the film.

Attempt should be made to determine the location of the foreign body, which is readily done if it is radiopaque. Intravesical or intrauterine foreign bodies should be ruled out before laparotomy is performed.

At laparotomy, most foreign bodies are easily found, particularly if search is directed toward the right side of the abdomen, the omentum, or areas of matted bowel. Small objects may present great difficulty. Another source of difficulty is lodgment of the foreign body in the retroperitoneal spaces, particularly the broad ligament. Uterine or cul-de-sac perforation is sutured in the absence of spontaneous closure by sealing over with fibrinous exudate or by omental or bowel adhesions. Careful inspection of the bowel is necessary to rule out perforation or other injury, even though this is uncommon. Drainage is not usually considered necessary, particularly with antibiotic therapy. Hysterectomy is not indicated; it may be considered in the presence of generalized peritonitis.

The prognosis is usually good because: (1) patients generally seek medical care soon after the perforation; (2) there is relatively minor injury to the uterus; (3) bowel injury is uncommon; (4) the omentum frequently plays an important protective role by enveloping the foreign body and localizing the inflammatory process; and (5) antibiotic therapy aids in controlling infection.

Addendum.—Since submission of this paper for publication, a report on the subject by Veprovsky and Ostreich[44] has appeared in this JOURNAL.

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BREECH DELIVERY AT THE CHICAGO LYING-IN HOSPITAL, 1945-1952*

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A SERVICE must periodically examine its records to determine whether the results are better or worse than they were previously and also to compare them with reports from other services. Breech delivery is evaluated (1) by the maternal deaths and injuries, both of which should be extremely rare, and (2) by the number of stillbirths, neonatal deaths, fractured long bones, and intracranial hemorrhages.

The senior author in 1946 reported a study of 638 breech deliveries with a corrected stillbirth and neonatal mortality for babies weighing 1,000 grams or more of 4.7 per cent and for 2,500 grams or more of 1.7 per cent. According to a recent unpublished survey made by Goethals these figures are as low as any that have been reported. Recent reports from various institutions give an uncorrected stillbirth and neonatal rate of from 4.9 to 42 per cent and a corrected loss of from 1 to 11 per cent.

The value of early obstetrical care is demonstrated in a study by Ludlam and Winchester, from the Edinburgh Simpson Maternity Pavilion, who reported for the period 1945 to 1949 an uncorrected stillbirth and neonatal mortality for 312 "booked" (prenatal care by hospital staff) primagravidas of 14 per cent and 103 "non booked" of 28 per cent. Comparable figures were 28 per cent for 155 "booked" and 42 per cent for 118 "non booked" multiparas. All patients were delivered by residents under supervision. The mortality for breech delivery in multiple pregnancy was 24 per cent. The uncorrected stillbirth and neonatal mortality for all babies in the hospital of 2¾ pounds or more during the same five-year period was 8 per cent. Of the total 688 single breech deliveries, 21 per cent of the infants were premature. Sixty, 13 per cent, of the 449 infants presenting by the breech in primagravid patients were delivered by cesarean section. There were 6, 10 per cent, neonatal deaths in this group.

Brown and Irvine from the same hospital reported that in multiparas a significant proportion had had a breech position in a previous pregnancy or pregnancies and 20 such patients had a combined perinatal mortality of 45 per cent. If the 180 past histories are reviewed, the perinatal mortality for all positions was 12.8 per cent. They noted that the higher perinatal loss found in breech extraction was due to the "mortality of delay."

Dieckmann, in a previous report, divided breeches into single (frank), legs extended and thighs flexed; and double (full, complete, foot, knee), legs and thighs flexed. He stated that all single or double footling or knee or any

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combinations were modifications of the double breech; and the presence of one or both feet made traction possible at any time, thus differing from the single type, where the "breaking up" of the breech becomes very difficult and at times impossible due to failure of the uterus to relax under deep anesthesia. He also stated that a nuchal arm did not occur unless the operator caused it. He described the management of the spontaneous breech and advocated delivery of the shoulders and head under anesthesia and of breech extraction for both single and double breeches if labor did not progress normally. We have seen no need for changing any opinions given in the previous report. All studies indicate that if the baby delivers vaginally as a breech the perinatal mortality is 3 to 8 times that for cephalic delivery. Table I lists comparisons of both types of positions by Calkins and by us.

TABLE I. COMPARISON OF CEPHALIC AND BREECH PERINATAL MORTALITY RATES IN PER CENT

WEIGHT (GRAMS)	CALKINS		CHICAGO LYING-IN		
	CEPHALIC	BREECH	CEPHALIC	BREECH	
	CORRECTED		UNCORRECTED		CORRECTED
1,000 +	0.5	4.0	1.8	7.5	3.2
1,500 +	0.4	3.5	1.2	4.9	1.4
2,500 +	0.3	2.2	0.6	2.3	0.9
4,000 +	1.2	5.0	1.0	0	0

Goethals, at the Boston Lying-in Hospital, has continued the excellent study of breech deliveries which he first reported in 1939. An unreported recent series of his, comprising 228 babies that weighed 2,500 grams or more, gave a corrected stillbirth and neonatal loss of 0.9 per cent, the same figure which we obtained in 754 similar babies. This is the mortality due to breech delivery.

Goethals divides breeches into two groups: (1) Cases complicated by any factor which in itself causes jeopardy to the fetus. Such factors include syphilis, diabetes mellitus, cardiac disease, pulmonary tuberculosis, tumors of the uterus or adnexa, pre-eclampsia, placenta previa, abruptio placentae, prolapse of the cord, and Rh-negative patients with anti-Rh titers. He states that in any such case the fetus is exposed to double jeopardy or to even higher jeopardy if two or more of the above factors should coexist. (2) Cases not so complicated. These are the cases in which the risk from the presentation alone and the method chosen for delivery can be computed. These cases are divided into two groups: (a) mature infants with birth weight of 2,500 grams or more, (b) premature infants with birth rates of 1,000 to 2,499 grams. (These are reported as groups with birth weights in multiples of 500 grams.) From the term and premature babies have been deducted those babies in whom no heart tones were heard at the onset of labor and all with gross malformations.

Table II shows the number of breeches for each weight group and their respective mortality according to Goethals' criteria, uncorrected and corrected. In 942 corrected breeches, the total stillbirth and neonatal mortality rate was 3.2 per cent. The perinatal loss of term babies was 0.92 per cent, *deaths due to the breech position.* As the weight of the baby decreased the mortality markedly increased and 58 per cent of the 1,000 to 1,499 group were lost. In the complicated group the perinatal loss was high in all groups and in the 1,000 to

1,499 gram group was 90 per cent; the total loss for all groups was 36.5 per cent. In the group corrected by Goethals' criteria there is again the high mortality, 32 per cent for the premature breech, and 0.9 per cent for babies that weighed 2,500 grams or more. The total corrected perinatal loss is 3.2 per cent for all babies of 1,000 grams or more. All subsequent data will relate to babies of this weight group.

TABLE II. BREECH DELIVERY: STILLBIRTHS AND NEONATAL DEATHS

WEIGHT (GRAMS)	UNCORRECTED		GOETHALS' CORRECTIONS						
			SIMPLE, UNCOMPLICATED		OMITTING ANTEPARTUM DEATHS AND MALFORMATIONS		COMPLICATED		
	NO.	%	NO.	%	NO.	%	TOTAL NO.	NO.	%
400- 999	27	96.3	—	—	—	—			
1,000-1,499	46	65.2	36	58.3	32	53.1	10	9	90.0
1,500-1,999	51	31.4	41	29.3	35	17.1	10	4	40.0
2,000-2,499	142	9.9	133	9.0	121	0	9	2	22.2
2,500-3,999	761	2.3	761	1.3	754	0.92	34	8	23.5
4,000 +	34	0		0		0			0
Total	1,061	9.8	971	5.7	942	3.2	63	23	36.5

Goethals deletes those cases in which there was a prolapse of the umbilical cord. This occurred 17 times, an incidence of 1.64 per cent. Six of the 17 babies were delivered by cesarean section with no fetal loss. In the remaining 11 cases 54 per cent of the babies were lost. We believe that prolapse of the umbilical cord is more likely to happen with a double breech than with a single or cephalic presentation, and question whether these babies should be deleted. If we include them, our perinatal (1,000 gram plus) loss is 3.7 per cent.

TABLE III. COMPARISON OF THE CORRECTED BREECH PERINATAL MORTALITY FOR TWO HOSPITALS

WEIGHT (GRAMS)	CHICAGO LYING-IN HOSPITAL						BOSTON LYING-IN	
	1941 — 1944		1945 — 1952		1941 — 1952		1938 — 1952	
	NO. CASES	PERINATAL MORTALITY %	NO. CASES	PERINATAL MORTALITY %	NO. CASES	PERINATAL MORTALITY %	NO. CASES	PERINATAL MORTALITY %
1,000-1,499	34	39.2	32	53.1	66	45.5	37	46.0
1,500-2,499	80	11.1	156	3.9	236	6.4	186	5.9
2,500+	524	1.7	754	0.9	1278	1.3	692	2.5
1,000+	638	4.7	942	3.2	1580	3.9	915	4.4
1,500+	604	3.0	910	1.4	1514	2.0	878	3.2

Goethals has permitted us to use his data for comparison. Table III shows a similar period of time. Our perinatal mortality for babies weighing over 1,000 grams is slightly lower, 3.9 versus 4.4 per cent and for term babies 1.3 versus 2.5 per cent. Our mortality in premature babies is also slightly lower, 10.8 versus 12.5 per cent for babies from 1,000 to 2,499 grams, but if babies weighing less than 1,000 grams are included his rate is lower.

Table IV shows the time and number of deaths: 22 per cent were antepartum, 22 per cent were intrapartum, and 56 per cent were neonatal. One thousand seventeen babies were alive at the onset of labor but 17 died during and 44 after labor. Conceivably these 61 babies (6 per cent) could have left the hospital alive, except for possible mistakes in judgment during labor, prematurity, major malformation, or maternal complications. Some of the deaths

were preventable or had preventable factors. Permitting the occiput to enter the pelvis posteriorly, forceps to the head above the pelvic brim, and traction on the neck, are all procedures to be condemned.

TABLE IV. TIME OF FETAL DEATH

WEIGHT (GRAMS)	UNCORRECTED FETAL MORTALITY, INFANTS THAT WEIGHED 1,000 GRAMS PLUS								
		DEATHS							
		ANTEPARTUM		INTRAPARTUM		NEONATAL		PERINATAL	
	NO. CASES	NO.	%	NO.	%	NO.	%	NO.	%
1,000-1,499	46	7	15.2	5	10.9	18	39.1	30	65.2
1,500-1,999	51	2	3.9	4	7.8	10	19.6	16	31.3
2,000-2,499	142	4	2.8	2	1.4	8	5.6	14	9.8
2,500+	795	4	0.5	6	0.8	8	1.0	18	2.3
Total	1,034	17	1.6	17	1.6	44	4.3	78	7.5

Fifty-four per cent of the patients were primiparas and 46 per cent were multiparas with 6.2 and 9.1 per cent perinatal deaths, respectively. The multiparas had a 50 per cent greater loss than the primiparas due to a higher percentage of premature babies. This is a reversal of fetal loss which is usually much higher in primiparas than in multiparas.

There were 686 (66 per cent) single (frank) breeches with a perinatal loss of 6.4 per cent and 348 (34 per cent) double breeches with a loss rate of 9.8 per cent. The higher number of premature babies in the latter group accounts in part for the increased rate. The early delivery of the foot or feet into the vagina but especially through the vaginal opening suggests that delivery is imminent. Unfortunately, the cervix is frequently not completely dilatable for the feet are smaller than the shoulders or head and the babies dies or is severely injured because of attempts to deliver through the incompletely dilated cervix.

Table V shows the perinatal loss for the various types of delivery. The spontaneous group had a higher loss because there were more small, premature babies in this group and more antepartum and intrapartum deaths. There is no appreciable difference between those born with manual aid and those born by extraction. Cesarean section, which was used in about 12 per cent of the cases for various indications, has an uncorrected perinatal mortality of 5.6 per cent, almost as high as that of the babies born by the vaginal route, but the corrected figure is 1.1 per cent. The lives of babies are of value but, despite our figures, we are opposed to the routine use of cesarean section in all breech positions.

TABLE V. METHOD OF DELIVERY (INFANTS OF 1000 GRAMS PLUS, UNCORRECTED)

METHOD	NO.	%	STILLBIRTHS AND NEONATAL DEATHS	
			NO.	%
Spontaneous	208	20.1	24	11.5
Manual aid	256	24.7	17	6.6
Extraction	447	43.2	31	6.9
Cesarean section	123	11.9	7	5.6
Total	1,034		79	7.5

Table VI lists the more frequent maternal complications associated with the delivery. We have used fewer bags than previously reported. The dilute intravenous Pitocin drip is now preferred. If there is doubt about a completely dilatable cervix, Dührssen's incision at 6 o'clock is advisable. Postpartum hemorrhage can be prevented by the intravenous drip of dilute Pitocin solution started

as soon as the placenta has been removed and the interior of the uterus explored. Note that 2 uteri were ruptured and treated by hysterectomy with both mothers surviving. Both babies had hydrocephalus; it was an unwarranted risk to attempt to deliver such babies without craniotomy. There were 7 craniotomies, the majority for hydrocephalus. One mentioned in the case report was a normal baby.

TABLE VI. COMPLICATIONS WITH DELIVERY

	NO. BABIES
Vaginal Vorhees bag	13
Placenta previa	10
Dührssen's incision	11
Rupture of uterus	2
Craniotomy	7
Postpartum hemorrhage	18

TABLE VII. INJURIES TO BABY

	NO. BABIES
Intracranial injury	11
Fracture of:	
Skull	1
Humerus	3
Elbow	1
Clavicle	5
Dislocation of hip	1
Brachial paralysis	1
Hematoma of muscle	1

Table VII lists the injuries to the baby. Twenty-three or 2.2 per cent, of the babies had injuries of some type. Sixteen, or 70 per cent, were delivered by breech extraction but the injuries in most part were due to lack of skill on the part of the operator. Of the 78 infants that were stillborn or died in the neonatal period, 11, or 15 per cent, had intracranial injuries. There are no diagnoses of intracranial injuries in any of the babies who survived. According to published reports, half or more of the babies born by breech who die show intracranial hemorrhage at autopsy. How many survive without clinical evidence is unknown. So far as we know there has been no follow-up of babies born by the breech to compare their subsequent course with those born by cephalic positions. Fractures of the skull, humerus, or elbow, or dislocation of the hip are inexcusable and are attributable to lack of experience. Fracture of the clavicle or brachial paralysis may occur.

TABLE VIII. INFLUENCE OF LENGTH OF LABOR ON FETAL MORTALITY

LENGTH LABOR (HOURS)	UNCORRECTED			CORRECTED (GOETHALS)		
		PERINATAL DEATHS			PERINATAL DEATHS	
	%	NO.	%	%	NO.	%
–2	3.5	1	3.2	3.7	1	3.3
2-6	34.0	28	9.2	33.7	9	3.3
6-12	40.4	34	9.5	39.8	13	4.0
12-18	12.8	4	3.5	13.2	3	2.8
18-24	5.6	2	4.0	5.8	2	4.5
24-30	2.6	2	8.7	2.6	1	4.8
30+	1.0	0	0	1.0	0	0
TOTAL NO. PATIENTS				TOTAL NO. PATIENTS		
909		71	8.0	850	29	3.6
CESAREAN SECTIONS				CESAREAN SECTIONS		
125		7	5.6	92	1	1.1

Table VIII shows the duration of labor and the perinatal loss. The loss with short labors was primarily due to the prematurity of the baby. Our corrected data do not show any increase in the rate with labors over eighteen hours. We consider a breech position as abnormal and watch such patients more closely.

TABLE IX. SADDLE BLOCK (LOW SPINAL) ANESTHESIA

	NO.	STILLBIRTHS AND NEONATAL DEATHS	
		NO.	%
Weight (Grams).—		3	42.3
1,000-1,499	7	0	0
1,500-1,999	6	1 (Meningocele)	6.7
2,000-2,499	15	0	0
2,500+	73		
	101		
Delivery.—			
Spontaneous	2		
Manual aid	16		
Breech extraction	83		
Inhalation anesthesia necessary 12			
	101		

Saddle block (low spinal anesthesia) was administered to 101 patients (Table IX). This was done primarily during the period when saddle block anesthesia was being evaluated and in some instances it was by mistake. Twelve patients required inhalation anesthesia in addition. There were 83 breech extractions. Spinal anesthesia did not increase the fetal salvage in the 1,000 to 1,499 gram group. Ether anesthesia is far superior to spinal anesthesia for a breech extraction because it will relax the uterus. We have not tried the curare group of drugs for additional relaxation of the pelvic muscles.

Forceps were applied to the aftercoming head in 547 cases with 21 deaths, an uncorrected perinatal mortality of 3.8 per cent. Ten of the 18 infants that died in the mature group had forceps to the aftercoming head. Six of the seven infants that died in the corrected mature group had forceps. Some of these forceps were applied to the head above the brim of the pelvis—high or floating forceps. These are inexcusable. If one cannot bring the head into the pelvis bimanually either in the anteroposterior, oblique, or transverse diameter under deep ether or chloroform anesthesia, forceps should not be used. They are as dangerous to the floating aftercoming head as they are to the forecoming floating head and it is better in such cases to sacrifice the baby than to take the chance of having it survive with an intracranial injury. The "combined" method of Dieckmann should be tried before a craniotomy is performed.

The morbidity rate was 8.1 per cent in 446 patients in whom the uterus was not palpated after delivery and 7.7 per cent if palpated, indicating the safety of this examination. The vaginal vault and cervix should be inspected and the interior of the uterus palpated after all deliveries of an aftercoming head. We have noted that patients who always have a breech position have a high incidence of arcuate or bicornuate uterus. Other obstetricians have made similar observations.

Treatment

The patient with a breech position of 33 or more weeks of gestation with ruptured membranes or in early labor should have a careful abdominal and vaginal examination and evaluation of the following: reproductive history, age, parity, pelvis, and size of the baby. An x-ray of the fetus and/or x-ray pelvimetry may be indicated.

The breech delivery in which dilatation and descent occur normally gives little trouble and the perinatal mortality will be low. In managing a breech delivery the doctor cannot wait until complications are present. He must know what can happen and must always be on guard to prevent or correct such complications. It is futile to wait until there is maternal distress, an impacted breech, a tonic uterus, or no advance of the presenting part; the majority of the babies at this stage will die, as illustrated in the Edinburgh report. Difficulties in the delivery of the breech are in achieving and/or recognizing a completely dilatable cervix and delivering the shoulders and head. If the doctor is experienced in the management of aftercoming shoulders and head, a breech extraction is no trouble for him. Rarely does the obstetrician have sufficient breech deliveries to maintain skill and it is advisable for him to practice elective internal podalic version and extraction.

Jarrett and Brandeberry in 1951 reported 445 internal podalic versions from the University Hospital of Western Reserve Medical School with an uncorrected perinatal mortality of 3.8 per cent and corrected of 2.2 per cent. They reviewed the recent literature and found that the maternal mortality in such cases ranged from 0 to 9.5 per cent and the corrected perinatal mortality from 2.3 to 38 per cent. They had no maternal mortality, no ruptured uteri, 4 lacerations of the cervix, and 5 cases of postpartum hemorrhage. Their experience demonstrates that elective podalic version does not appreciably increase the perinatal loss and gives experience in the management of the shoulders and head in breech delivery.

If the descent of the breech has been normal, when it crowns the perineum is infiltrated with 0.5 per cent Novocain, an episiotomy performed, and as soon as the breech is stemmed under the symphysis, the patient is anesthetized, preferably with drop ether, and the remainder of the delivery is completed by the physician without aid from the patient. We do not approve the Mauriceau-Smellie-Veit or Prague maneuvers because of the danger of intracranial hemorrhage. The Celsus-Wigand-Martin maneuver is effective in most cases in engaging the head either in the posterior, oblique, or lateral diameters of the inlet and delivery can be easily completed. Where it fails, the "combined" maneuver should be used, but the head should be in the pelvis. The delivery is more easily accomplished and there is less trauma if the "combined" maneuver, described by Dieckmann, is used (forceps are applied by one operator, the other, with the baby straddling his forearm, pushes the head from above, and at the same time flexes the baby's head with his fingers in its mouth).

Analgesic drugs should be used with caution. Gas inhalation for contractions is less likely to disturb the uterine mechanism.

Delivery should be by elective cesarean section in cases of (1) contracted or borderline pelvis, (2) probable cephalopelvic disproportion because of a baby estimated to weigh over 4,000 grams and a primiparous mother over 30 years of age, and (3) previous breech delivery with dead or damaged baby.

If the pelvis is normal and the baby is estimated to weigh less than 4,000 grams, the obstetrician is guided primarily by the length of time it takes for the cervix to dilate. If the uterine contractions are irregular, weak, and of short duration, decision should be made after six to eighteen hours of labor and/or ruptured membranes for either: (1) vaginal delivery or (2) cesarean section. If the baby is alive at the beginning of labor the obstetrician has used poor judgment if he delivers a dead or badly injured baby.

If the cervix becomes completely dilatable but the breech remains at the pelvic inlet, it is best to anesthetize the patient to surgical anesthesia with drop ether or chloroform, break up the breech, and complete the delivery. It is best to obtain both feet but if one is not certain about the dilatability of the cervix

then obtain only one foot and continue the delivery of the baby. When the feet are through the vulva a deep episiotomy should be performed. The delivery should be slow, with traction in the proper planes. It is best gently to rotate the posterior shoulder anteriorly, when, with slight traction, the scapula will appear under the symphysis. The fingers can then be used to splint the humerus and the arm delivered. The other shoulder is then rotated anteriorly and similarly delivered. One rarely has to pull the posterior shoulder into the pelvis and then rotate anteriorly. We do not believe a nuchal arm ever occurs spontaneously; it is the result of the obstetrician's inexperience.

Every physician *who keeps records* makes mistakes. Several short abstracts of mismanaged breech deliveries illustrate some of the mistakes. Cesarean section is not always the proper treatment; even though the corrected figure for all breech deliveries by cesarean section was 1.1 per cent, the neonatal mortality for all elective sections in our hospital is 4.5 per cent.

Patient No. 455768 was a 29-year-old gravida ii, para i, at term June 17, 1949. Her previous pregnancy terminated as a spontaneous breech delivery in 1947 after twenty hours of labor. The infant weighed 4,100 grams. Her present labor began at 2 P.M. and she was admitted to the hospital at 6 P.M. on June 29 at 42 weeks' gestation. The position was uncertain and x-ray examination showed a double breech and a normal infant. A vaginal examination at 7 P.M. revealed a double breech at the inlet and 1 cm. dilatation. The contractions were weak and at irregular intervals but nothing was done for 17 hours when, on June 30, at 11 A.M., a consultant advised the insertion of an 11 cm. Voorhees bag into the vagina and fractional doses of solution of posterior pituitary. The bag was to be removed in 8 to 12 hours. The cervix was 5 cm. dilated at 2 P.M. when the bag was inserted. The contractions became moderately strong at three-minute intervals. The bag was not removed until 10 A.M. on July 1, when there was 7 cm. dilatation with a very soft cervix. At 3 P.M. the cervix was reported completely dilated and under drop ether anesthesia the baby was delivered to the head. The latter could not be flexed because of the tightly contracted lower uterine segment. The consultant objected to forceps which would have caused a uterine rupture. The head was collapsed and delivered without difficulty. The bag should have been removed in 12 hours maximum and delivery completed then or several hours later when the cervix was completely dilatable. This case had preventable factors.

Patient No. 303679 was a 33-year-old gravida iii, para ii, who had a breech delivery in 1943 at 36 weeks' gestation. The infant, who weighed 2,000 grams, died in the early neonatal period and was found to have polycystic kidneys. This pregnancy in 1948 was terminated after an eleven-hour labor by a very difficult breech extraction because of a greatly distended abdomen. After the body was delivered it was found difficult to bring the head into the pelvis. Further examination revealed a hydrocephalic infant that was then delivered by craniotomy. Manual exploration of the uterus revealed a large rupture which extended into the broad ligaments. An immediate hysterectomy was performed. Autopsy of the infant revealed in addition to the hydrocephalus that the greatly enlarged abdomen was due to very large polycystic kidneys. The obstetrician and consultant each have consultant status and it is difficult to understand the injuries to the mother. Despite poor obstetrical care the patient was discharged alive.

Patient No. 410457 was a 27-year-old gravida ii, para i. She was admitted on May 27, 1951, at 42 weeks' gestation in active labor with ruptured membranes. After five hours of labor a vaginal examination showed complete dilatation, a double breech, and a concealed prolapse of the umbilical cord. After 20 minutes of ethylene and ether anesthesia an extraction was performed. The head was allowed to enter the pelvis with the occiput posterior which the operator then could not turn, hence he delivered the aftercoming head as an occiput posterior with the Simpson forceps. Such a delivery is always traumatic to mother and baby because of the extended head. The latter was stillborn and autopsy revealed bilateral fractures of the humerus and an intracranial hemorrhage in a 3,215 gram infant.

Summary

Our corrected stillbirth and neonatal mortality rate of 3.2 per cent for babies weighing over 1,000 grams is less in 1,034 breech deliveries for the period 1945 to 1952 than it was for the period 1941 to 1944. Even though our uncorrected and corrected losses are no higher than those reported in the literature, at least a third, and possibly more, of our intrapartum and neonatal fetal deaths had preventable factors. This does not mean that all of these patients should have been delivered by cesarean section.

Our corrected perinatal rate for term babies delivered vaginally is 0.92 per cent, while a comparable figure for cesarean section happens to be 0 per cent; thus if all had been delivered by cesarean section the rate would be appreciably lower. In reviewing our records of neonatal deaths which were preventable or had preventable factors, we find that in every instance the fetal loss can be charged to lack of training on the part of the operator. Some of the obstetricians have national reputations, but the number of breech deliveries by any one man in the period of a year is extremely small, and unless he maintains his skill by elective podalic version and extraction he will inevitably lose certain babies born by breech.

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Discussion

DR. FRANK E. RUBOVITS.—I have obtained the statistics from Michael Reese Hospital and the Chicago Maternity Center. I am able to make comparisons on the basis of gross figures only. For a comparable period of time at Michael Reese Hospital, there were 677 breech deliveries. The gross fetal loss—stillborn and neonatal—was approximately 7 per cent. These figures compare favorably with the figures of the essayist. The point of view of the group of obstetricians delivering these patients is mixed as to the optimum technique of breech delivery, i.e., some of the groups are proponents of breech extraction; others are proponents of spontaneous breech delivery with manual aid, in the absence of rigid indications for extraction.

At the Chicago Maternity Center, the statistical figures are significantly higher. Again, for a comparable period of time, there was a total of 740 breech deliveries. The gross fetal loss, stillborn and neonatal, was 22 per cent. Because of its magnitude, this figure was promptly subjected to further interpretation and certain observations come to light.

First, the patient group consists of the less fortunate consumers of obstetric service. For instance, 20 per cent of these patients were unregistered and were first seen by a physician at the time of delivery. Second, 12.5 per cent of these patients delivered unattended. Third, and probably most significant, 38 per cent of these patients delivered premature and previable premature infants that weighed 2,500 grams or less. Interpolating from Dieckmann's percentage statistics, 25 per cent of his group were premature. As has been indicated this evening, the major area of fetal loss in breech, or for that matter in any other type of delivery, is in the undersized infant.

There is no question but that in the two groups of patients which I have chosen to compare with Dieckmann's series obstetric mishaps occurred. We concur in the opinion that the obstetrician-in-training must become skilled in the technique of breech extraction. We concur that the so-called "teaching version and breech extraction" is justifiable if case selection is exceedingly circumspect. While it is true that the occasion for breech extraction is relatively infrequent in the case load of any obstetrician, I cannot help but feel that once the principles are understood and the practice obtained, the art is not soon lost.

To return to the gross figure of 22 per cent loss at the Chicago Maternity Center, let us allow that 2 or 4 or even 6 per cent of this loss may be ascribed to the trying obstetrical situation in which a relatively unskilled doctor might find himself. This still leaves us with a dismaying infant mortality. The progressive improvement in results then must come from at least two sources. One, of course, is the optimally skillful obstetrician. The other apparently is in progressive and, I hope, rapid further distribution of better medical care. This improvement must extend not only to the immediate obstetric situations but must extend to the total health and educational picture of a significant segment of our population who either do not seek out or cannot obtain the excellent obstetrical services available in the major institutions of our city. Only then, I think, will the over-all fetal salvage in breech delivery improve tremendously and this less from the standpoint of any particular technique of breech delivery; more from the standpoint of vigorous women with vigorous babies.

Another factor which needs discussion is the problem of anesthesia. We have heard on this platform and elsewhere that any anesthetic technique introduced into obstetric practice is a calculated risk. For the performance of breech extraction, a level of anesthesia of intensity, depth, and hazard is required exceeding that necessary for spontaneous breech delivery with manual aid. This, I feel, introduces a potential maternal hazard which we must not ignore.

DR. IRVING F. STEIN, SR., Chicago, Ill.—The doctor who can safely deliver a breech in a primipara is a good obstetrician. Before attempting delivery, however, he must make an accurate diagnosis. This includes not only whether the presentation is breech, but whether it is a single or complete breech. Roentgenography which has been used in pregnancy for many years is particularly helpful in breech presentation. The single breech is a form of deflexion attitude in which the legs are extended, the arms are often away from the trunk, and the spine is straightened and head deflexed. The head is extremely mobile in breech and may be turned as much as 180 degrees. When you have complete breech, or double breech, as Dr. Dieckmann called it, you may expect spontaneous delivery. However, in frank or single breech, just as with the deflexion attitudes, difficulty in delivery is usually encountered. It is quite definite that the deflexed cases of frank breech do not lend themselves to external version.

Roentgen examination is also extremely useful in multiple pregnancies when one or more fetus usually presents as a breech. In twin pregnancy, sometimes one is breech and one is transverse; one breech occurs in about 35 per cent of twin pregnancies. The roentgenogram is useful in determining the type of delivery needed for the first fetus presenting as breech and to prepare the physician for podalic version on the transverse second twin.

Finally, in the case of monstrosities such an anencephalic monster breech presentation may pose a delicate delivery problem. Here we see the anencephalus with extremely deflexed spine and very large trunk. In cases of hydrocephalus, the large aftercoming head presents a serious problem which can be predicted by the x-ray.

I wish to emphasize again that with a well-flexed fetus presenting as a breech, spontaneous delivery is the rule requiring only the usual manual aid to deliver the arms and head. With the frank breech, or deflexed fetus, extraction is more frequently required.

DR. HAROLD MORGAN, Lincoln, Neb. (by invitation).—I have been interested in the management of breech presentations ever since Dr. Hansen published his paper in 1941.

Dr. Harrod made the remark that the management of the breech depends upon certain manipulations of the infant. That is the way we in our group—and we all are practitioners of obstetrics—feel in our community. We feel that expertness is so necessary that perhaps it does not all rest in the hands and in the mind of one of us, but rather that two can do the job better than one. Consultation is required in the three hospitals in Lincoln. Those of us who are confining our efforts to obstetrics feel it is our duty to assist in the management of actual breech presentation. When a patient is delivered by the breech, there are always two obstetricians present at the delivery. We subscribe most heartily to the concept first published by my former associate, Dr. Hansen, which is epitomized by the fact that the pressure comes naturally from above and not from below. Therefore, in our series of 500 consecutive cases, there was a corrected fetal mortality of 1 per cent, and we have felt that we have demonstrated the validity of our opinion that expert assistance is necessary. We have at no time utilized external version in the management of 500 cases. Our cesarean section incidence is 3 per cent. We feel that cesarean section is lifesaving as far as the baby is concerned. If no progress has been made in labor, particularly in a breech in an elderly primipara, cesarean section is indeed lifesaving.

The points I wanted to emphasize are, first, we do no external versions prior to delivery and, second, we do very few extractions; about 80 per cent of our patients with breech presentations are delivered by manual aid.

DR. C. O. McCORMICK, Indianapolis, Ind. (by invitation).—We all agree breech delivery has a recognized associated mortality, even when conducted by a specialist. Then, too, the necessity of an able assistant, surgical anesthesia, and a pair of forceps makes the breech presentation a pathological entity.

An x-ray should be routine in a suspected or known breech presentation in order to confirm the diagnosis, to diagnose the variety of breech, and to discover a possible etiological abnormality. Another very practical aid in diagnosing the breech is the maneuver described by Mengert, which consists of steady pressure applied with extended fingers and thumb to the presenting pole, while we are steadying the top of the fundus with the other hand and having an assistant note the rate of the fetal heart. If the rate decreases as the pressure increases, the breech is presenting.

Considering the increased mortality and morbidity associated with breech as compared with cephalic presentation, we are in agreement with Dr. Morgan that external version is a valuable and important prophylactic procedure, and we apply it almost routinely, guarding against such contraindications as previous section, multiple pregnancy, bicornate uterus, uterine fibroids, rutured membranes, placenta previa, tonic uterus, anencephalic monster, etc.

We believe the external version can be performed with less failure if done under deep ether anesthesia and with the aid of an assistant. Where anesthesia is indicated, as is the case when dealing with most primiparas and some multiparas, the uterus should be anesthetized as well as the patient, that is, it should be well relaxed. Gas does not afford this relaxation and when used accounts for many failures, and it is our belief it is more conducive to possible trauma. It is our experience and belief the operation is not always afforded its just due when performed by the attendant alone.

Briefly our technique is as follows: The patient, having been anesthetized and the abdominal surface freely powdered with talcum, is put in the Trendelenburg position. If the breech is engaged it may be necessary to push it up out of the pelvis with two fingers in the vagina. Otherwise it is lifted or pulled up into the false pelvis by the fingers of both hands of the attendant, the force being applied to the ventral surface of the breech. Then the breech is lifted upward out of the false pelvis, and the assistant then, and not until then, likewise applies the fingers of both hands to the dorsum of the head now located in the opposite upper quadrant. Both operators apply pressure synchronously until the infant lies in the transverse position. The maneuver is then readily completed by continued pressure rotating the body off center.

These maneuvers are performed intermittently and with leisurely gentleness, being completely omitted during uterine contractions and slowing of the fetal heart. Also, the abdominal wall is protected by the removal of "steel" from the fingers, and allowing the finger tips to glide over its powdered surface.

Some outstanding authorities claim external version does not cut down the incidence of breech presentation. This is contrary to our experience. Perhaps this is due to our repeatedly performing the version in those cases where the baby reverts to breech after the turning. It may also be due to our greater incidence of success. We prefer to do the version at twenty-eight to thirty weeks but often perform it successfully near and in some instances even at term. The danger of wrapping the cord about the baby is no greater than with a spontaneous version; besides, the possibility of unwrapping the cord is almost as great as of wrapping it about the baby. We hold prophylactic external version as particularly indicated in handling premature deliveries with breech presentation.

The essayist referred to the Voorhees bag, and stated the usual, and perhaps just, disclaim for it. I would like to ask him if he does not think it has a practical place in dealing with breech prematures, the idea being to spare the head all possible molding, and thereby prevent or at least reduce intracranial hemorrhage.

DR. PHILIP J. STEIN, Chicago, Ill. (by invitation).—I wonder whether the essayists would elaborate a little further on the use of intravenous Pitocin in desultory labor in breech delivery.

DR. HARRY BENARON, Chicago, Ill.—The authors are to be congratulated on as low a fetal mortality as any reported. Such excellent results are achieved by day in and day out work in the prenatal clinics, by the efficiency in the labor line, and by intensive and expert supervision in the delivery rooms.

I believe the essayists did not sufficiently stress the value of prenatal care in the elimination of fetal mortality. They mentioned the Edinburgh series as showing 14 and 28 perinatal mortality, respectively, in booked primiparas as against booked multiparas. In nonbooked primiparas it was doubled, or 28 per cent, and in nonbooked multiparas, 42 per cent. It is apparent that the patient with a breech presentation who has not availed herself of the advantages of prenatal care has the cards stacked against her. It is my opinion that the patient with a breech presentation, in the majority of instances, should have the benefit of x-ray pelvimetry. Morphology and capacity can be defined where the clinical hand cannot reach.

It is interesting that two-thirds of the presentations were single breeches, and one-third were double. Do the authors have an explanation for the preponderance of the single breech over the double variety? In the etiology of breech presentation many authors list multiparity as a factor, yet here we are presented with 54 per cent primiparas and only 46 per cent multiparas. Is the hospital population similar?

Postpartum hemorrhage is reported only 18 times, yet 447 breech extractions were done. This is remarkable, inasmuch as the authors use deep surgical ether for their anesthetic of choice and deep ether notoriously predisposes to postpartum hemorrhage. In the series 78 fetal deaths are reported and yet only 11 deaths from intracranial hemorrhage. This is contrary to published reports on the incidence of intracranial hemorrhage in stillborn infants following breech delivery or extraction, some authors placing it as high as 75 per cent (Holland).

Dr. Dieckmann uses the term "completely dilatable" cervix. I think this is a dangerous teaching and will get one into more trouble than any other one factor. In breech extraction, extended and nuchal arms may well result from not waiting until the cervix is both completely dilated and also retracted. Where a high single breech, in an adequate pelvis, will not engage and pull up the last few centimeters of cervix, I prefer a two-stage procedure—break up the breech by bringing down the anterior leg, and await complete dilatation and retraction which usually follows this step. An extraction if indicated can then be done.

A rather novel means for delivery of the aftercoming head is presented as the "combined method of Dieckmann." In this I see no merit whatsoever, since properly applied forceps serve better, both to flex the head as well as to extract it.

The authors point out that no individual ever gets enough breeches to sharpen his skill. They suggest that elective version and extraction be done, quoting the series of Jarrett and Brandenberg of 445 podalic versions. Yet this highly selected series, with fetal heart tones present and an adequate pelvis, resulted in a perinatal uncorrected mortality of 3.8 per cent, and a corrected rate of 2.2 per cent. Is this not too high a price to pay for experience? I believe that the operation of breech extraction is a very serious one, that it is a major procedure, and is not to be recommended lightly.

At the Chicago Maternity Center we had 938 babies born by the breech from 1945 to 1954. One mother died of postpartum hemorrhage following a breech extraction. Of these 938 deliveries, 117, or 12.47 per cent, were unattended, the patient having failed to call in time, or being unable to get other medical care. The uncorrected stillbirth and neonatal death rate for the 938 cases was 22.92 per cent, including babies under 1,000 grams. In one selected five-year period (1945-1949) there were 49 neonatal deaths; 37, or 75 per cent, of them were premature and 5 others were from unattended births. In that same period there were 66 stillbirths; 44, or 66 per cent, of them were premature, and 16, or 24 per cent, were unattended. In this five-year period there were 115 stillbirths and neonatal deaths, and of these 81, or *70 per cent,* were premature, and 21, or 18 per cent, were actually unattended for the second stage of labor.

DR. WILLIAM G. CUMMINGS, Evanston, Ill.—Because the delivery of a breech is more of a challenge than of a cephalic presentation, I am sure we have all enjoyed this interesting paper. Certainly, such excellent results as these and others reported in recent years demonstrate that breech delivery need not carry with it the much higher fetal mortality and morbidity rates previously considered as average.

The results, as reported, will vary not only with the skill and care in managing these patients, but also with the criteria used for reporting fetal mortality.

Certainly, the babies who weigh 2,500 grams or more are the important group to consider in this connection. The mortality in smaller babies results in a very large degree from prematurity and fetal anomalies that are not a result of breech delivery.

At the Evanston Hospital in a little over twelve years, ending August, 1954, there were 605 breech births. This represented 3.33 per cent of total births. Including only babies over 2,500 grams, there were 3 deaths for a corrected rate of 0.49 per cent as compared with 1 per cent for all births. In a series from the same hospital reported in 1938, the corrected fetal mortality was 7.3 per cent, as compared to 3.5 per cent for all births.

There must be a reason for this much improvement. I am not sure I know all the answers to this, but certain factors are worth mentioning.

Routine external version has been advocated by many. It caries some drawbacks and hazards which are familiar to us all. In any teaching hospital as many breech presentations as possible are needed for instruction of residents.

Better anesthesia surely accounts for some improvement in results. For a breech extraction, proper uterine relaxation is of tremendous help. I believe breech extraction should be done only when indicated and with full cervical dilatation.

Cesarean sections are done for the usual indications and seldom for breech presentations as the only indication.

Perhaps the greatest factor is the much more liberal use of forceps on the aftercoming head. Intracranial injury is the commonest cause of death in these babies. Proper use of forceps on the head can protect the head during its delivery and I believe they should be used almost routinely.

DR. DIECKMANN (Closing).—The obstetrician who has never made a mistake either has not practiced or has a very poor system of records. Many men, particularly in managing breech deliveries, use "masterly inactivity," "hands off," "give nature time," etc., which I think indicates the doctor's inherent fear of the possible outcome in the hope that such a policy will give the best results. We mentioned the very high perinatal mortality which ap-

peared in the "nonbooked" cases in Scotland. Dr. Rubovits gave similar figures for the Chicago Maternity Center with reference to patients who were delivered unattended, in which cases there was certainly "masterly inactivity," and "hands off."

The art in obstetrics is to know what complications might develop, and to be able to prevent their occurrence or correct them early enough before damage has occurred to mother or baby, or even death to one or the other. Dr. Cummings' results are excellent; I believe all are private cases. Dr. Morgan has emphasized the importance of two obstetricians being present at each breech delivery. That is, a team is present for this complication. I have been urging the use of teams for all complications in obstetrics and gynecology. Very few obstetricians have a sufficiently large private practice to ensure skill in the less frequent complications.

Dr. McCormick uses ether anesthesia and external cephalic version in primigravidas. I wonder how many of them change back to a breech. We teach our students and residents external cephalic version, but do not practice it, for we want the cases for training. External version under anesthesia may cause placental separation or fetal strangulation from the cord.

Dr. Benaron stated he could see no need for the combined maneuver. It is difficult even with the forecoming head to maintain maximum flexion with the ordinary forceps with a pelvic curve. It is impossible with the aftercoming head with any type of forceps which I have tried, even the Piper, to achieve, much less maintain, proper flexion. It is surprising how easy the delivery is, if forceps are applied for traction, and flexion is achieved by abdominal pressure and pressure on the baby's jaw. His comments concerning prenatal care are pertinent, although delivery care is still the most important. We mentioned the need for having a completely dilated or dilatable cervix. Failure to recognize such a condition not only results in extended arms, but in a trapped head, on which pressure or forceps usually result in a ruptured uterus and a high incidence of intracranial injury.

The doctor should have a definite plan in mind as to the management of every delivery, and this is of the utmost importance if the presenting part is a breech. If he lacks proper skill, he should obtain early consultation. A visit to one of the Chicago special schools for the physically handicapped where one-third of the children have cerebral palsy will convince him of the wisdom of proper consultation.

HYDRAMNIOS

A Review of 204 Cases at the Sloane Hospital for Women

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WITH the development of techniques using radioactive isotopes for clinical investigations, there has been a renewed interest in the physiology of amniotic fluid circulation in both normal and pathological cases. In addition, the technique of transabdominouterine taps in cases of hydramnios has enabled investigators to use this method both therapeutically and experimentally under various circumstances.[1, 2]

Apart from some of these more recent studies, the literature shows a paucity of collected clinical material. The work of Mueller[3] in 1948 analyzed a series of 62 cases at the New York Lying-In Hospital. The earlier report of Taussig[4] presented his experience in 32 cases. These two articles represent the total of reported material in the American literature since 1927. Occasional case reports have appeared from time to time.

Advances in surgical techniques, and in particular in the surgery of the newborn infant, have made it necessary to study the various congenital anomalies afflicting the infants born of mothers suffering from hydramnios, with the hope that prompt and effective surgical treatment might be curative in a certain proportion of such cases.

With this purpose in mind and to obtain clinical background material for some of the experimental studies in the circulation of amniotic fluid, it appeared worth while to review the experience at the Sloane Hospital for Women from 1935 to 1952.

Material

The cases of hydramnios were reviewed with special reference to the prenatal factors, labor, delivery, puerperium, and fetal mortality. All the infant records were secured, and notations about the immediate neonatal period were made. Follow-up data on these babies were available, ranging from one month to adulthood. The autopsy incidence, as will be noted later, was high. Since it is the practice at the hospital to perform meticulous postmortem examinations, a complete study of fetal anomalies and malformations was possible.

A total of 204 cases were reviewed after discarding 22 ward and 16 private records because either they lacked convincing evidence of hydramnios, or the clinical data were inadequately documented. It must be stated here that hydramnios is essentially a clinical diagnosis, and the milder cases may

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offer difficulties in recognition. Hence, the policy was adopted to include in this series only those cases in which the diagnosis had been substantiated by one of the attending obstetricians.

The over-all incidence was one in 168 cases. This is somewhat at variance with the incidence reported by Mueller at the New York Lying-In Hospital, of one in 754 deliveries. Similarly, at the Johns Hopkins Hospital[5] an incidence of hydramnios of 1 in 358 was reported. Our present figures, however, are in accord with those obtained at the old Sloane Maternity Hospital (Cragin's[6] *The Practice of Obstetrics*) of 1 in 177.

The cases of acute and chronic hydramnios have been analyzed together. While textbooks make the differentiation between the acute and chronic varieties, we have seen no real necessity of following it. It is our belief that it is the degree and severity of the condition that really matter, rather than the rapidity of onset.

TABLE I. PARITY, AGE, RACE

	NO. OF PATIENTS	%
Parity.—		
Multiparous	117	57
Primiparous	87	43
Age (years).—		
15-19	4	
20-24	46	
25-29	56	
30-34	57	
35-39	30	
Over 40	11	
Race.—		
White	140	68.5
Negro	64	31.5

Parity, Age, and Race.—

The distribution of cases according to parity, age, and race is noted in Table I. For comparison, during the period under discussion the incidence of primiparous patients in the total obstetric group was 45.7 per cent and the white patients constituted 73 per cent of the service. There is, therefore, no significant difference among patients with hydramnios relative to these factors. The women over 40 years old constitute 5.4 per cent of this study group in contrast to the service figure of 3.4 per cent.

Rh Factor.—

Since Rh determinations became a standard laboratory procedure, they were done on all patients who have been included in this series, a total of 99 Rh determinations. Eighty-eight patients were Rh positive and 11 were Rh negative. Of the 11 who were Rh negative, 5 had evidence of incompatibility with elevated agglutinin titers. The fetal end result in these 5 showed 2 erythroblastotic stillborn infants, 1 unexplained stillbirth of a macerated infant, 1 unexplained intrapartum death, and 1 anencephalic monster.

The incompleteness of the Rh determinations makes any deductions highly speculative. It is striking, however, that the incidence of Rh isoimmunization among the group with incompatible matings (45 per cent) is higher than usual. It has been stated[5] that the general incidence of isoimmunization among Rh-negative mothers is approximately 5 per cent.* What the probable relationship

*Applying the formula $X^2 = \frac{(ad - bc)^2 \ (a + b + c + d)}{(a + b) \ (c + d) \ (a + c) \ (b + d)}$, a test of independence, these figures are statistically significant with a probability of less than 0.01 ($X = 35.4$, $n = 1$). However, it is apparent that the quoted series is small.

is between this high incidence of Rh immunization and the development of hydramnios, we are not prepared to answer at present. Further work along this line would be of interest.

Syphilis.—

Among the 204 cases of hydramnios, 7 patients had a positive serologic test for syphilis. Among these, 6 cases were diagnosed as latent syphilis, and 1 as asymptomatic neurosyphilis. All patients were treated prior to delivery adequately enough to ensure a healthy baby under ordinary circumstances. The incidence of syphilis in this series was 3.4 per cent. The over-all incidence of syphilis during the same period of time on the obstetric service was 2.2 per cent. It appears quite certain that there is no etiological relationship between syphilis and hydramnios.

Severity of Hydramnios Correlated With Time of Onset.—

It becomes clearly apparent, after a review of the series, that the more severe cases behave differently from the mild ones. With this in mind, all cases were analyzed as to the severity of the symptoms and were arbitrarily divided into 3 types: (1) the severe cases, (2) the moderately severe cases, and (3) the mild cases. For the purpose of classification, the severe cases included those with dependent edema, dyspnea, tenseness of the abdomen, inability to palpate the fetal parts, and amniotic fluid in excess of 5,000 c.c. Included among these are the cases of "acute" hydramnios. The mild cases were classified as such when there was very little or no physical discomfort; when amniotic fluid did not exceed 3,000 c.c. and still the patient had evidence of abdominal tenseness, ballottement of the fetus, and increased size of the uterus. Cases falling between these two categories were diagnosed as moderately severe cases.

TABLE II. ONSET OF HYDRAMNIOS

WEEK DIAGNOSIS MADE	SEVERE CASES		MODERATELY SEVERE		MILD CASES	
	NO.	%	NO.	%	NO.	%
18-21	1	1.8	1	1.3	1	1.3
22-25	2	3.7	0	0	1	1.3
26-29	14	25.9	6	8.2	2	2.9
30-33	20	37.0	22	30.1	11	16.4
34-37	13	24.0	31	42.4	18	26.0
38-42	4	7.4	13	17.8	34	50.0
Total	54		73		67	

The time of appearance of hydramnios was taken from the clinic record and refers to the date that the diagnosis was first made. This is shown in Table II. A total of 194 cases were available for computation of the time of onset of the disease, divided into 54 severe, 73 moderately severe, and 67 mild cases. It will be noted that the peak incidence of the severe cases occurs between the thirtieth and the thirty-third weeks. The moderately severe cases reach their peak later, between the thirty-fourth and the thirty-seventh weeks, while the mild cases appear still later in maximal number at or after the thirty-eighth week. Thus it may be stated that the earlier the time of appearance of symptoms of hydramnios, the more severe it is likely to be. Cases appearing before the thirtieth week will have a greater probability of being severe.

Associated Complications of Pregnancy.—

The associated complications of pregnancy in the series are shown in Table III. It will be noted that the incidence of pre-eclampsia is 15.6 per cent and that for hypertensive cardiovascular diseases, with or without superimposed toxemia, is 9.7 per cent. This is about three times the expected inci-

dence of these conditions as noted in our clinic population. The incidence of pre-eclampsia and hypertensive vascular diseases in the general clinic population during the period under consideration was 9 per cent. The incidence of diabetes in this series was 2.4 per cent, which is significantly higher than the 0.31 per cent incidence of diabetes during the same period of time in the clinic population. This agrees with the reports of other writers who give higher incidences of diabetes and hypertensive toxemias in cases of hydramnios. While there is no significant difference in the cardiac group, it will be observed that the incidence of myomas of the uterus is higher in hydramnios. This raises the question of the possible etiological relationship of myomas to hydramnios. It would be interesting to study these relationships further, but it is not within the scope of the present communication. It may be added that the inability to show any increase in cardiac complications is contrary to the suggestions that increased venous pressure may be a factor in the etiology of hydramnios.

TABLE III. ASSOCIATED COMPLICATIONS OF PREGNANCY

COMPLICATIONS	NUMBER	%	AVERAGE INCIDENCE AT SLOANE HOSPITAL
Pre-eclampsia	32	15.6	9
Hypertensive vascular disease	20	9.7	
Hyperemesis gravidarum	5	2.4	1
Fibromyomas of the uterus	12	5.8	3.5
Threatened abortion	3	1.4	
Diabetes mellitus	5	2.4	0.31
Cardiac disease	7	3.4	3.2
Anemia	9	4.4	7.5
Rheumatoid arthritis	3	1.4	
Neurological disease	3	1.4	
Psychiatric disease	1	.48	
Goiter	1	.48	
Asthma	1	.48	

Multiple Pregnancies.—

There were 13 sets of twins in the series, an over-all incidence of twin pregnancy of 6.3 per cent. In all instances the hydramnios occurred in the sac of the second twin. Eight of the patients had severe hydramnios. Two had moderately severe hydramnios and 3 had the mild form. Of the 26 babies born there was a total fetal mortality of 61 per cent (9 neonatal deaths, and 7 stillbirths). Ten babies were born alive and were well at follow-up. This 6.3 per cent incidence of twinning is significantly higher than the incidence of multiple pregnancies in the general clinic population for the period under consideration, which was 1.5 per cent. Thus, twin pregnancy occurs 4 times as often in cases of hydramnios.

There was only one patient with triplets, in a severe case, but there was no information as to which sac had the hydramnios.

Weight Gain.—

In 167 cases, data on weight gain during pregnancy were available. The weight gain is reported as the difference between the prepregnancy weight and that noted at the last clinic visit. Weight gains ranged from a minimum of 2 pounds to a maximum of 67 pounds, an average of 24.8 pounds per patient. This is not significantly different from the usual weight gain seen in normal patients.

Labor.—

The week of onset of labor in these patients is shown in Table IV. The high incidence of prematurity is obvious. Of the patients under considera-

tion, labor was spontaneous in 161 and was induced in 39 because of extreme discomfort or for other reasons. Of these inductions, 7 were done with Pitocin, 15 by rupture of the membranes, 7 with Pitocin and rupture of the membranes, and 10 with castor oil and quinine. There were only 2 failures. These occurred in the castor oil-quinine group. Induction of labor in these patients does not appear to be harmful by any of the present methods, and carries no increased risk of prolapse of the cord or separation of the placenta, as will be noted later.

TABLE IV. ONSET OF LABOR

WEEK OF ONSET	NUMBER OF PATIENTS*	%
38-42	115	57.5
32-37	67	33.5
26-31	15	7.5
20-25	3	1.5

*No information available on 4 cases.

The duration of labor in 186 patients with hydramnios who delivered vaginally did not differ significantly from the average. There were only 3 labors of over thirty hours, an incidence of 1.6 per cent.

TABLE V. COMPLICATIONS OF LABOR

COMPLICATIONS	PRESENT SERIES (%)	SLOANE HOSPITAL 1935-1952 (%)
Prolonged labor (over 24 hours)	4.8	6.45
Intrapartum uterine inertia (first and second stages)	2.1	3.11
Third-stage uterine inertia	0.49	1.05
Postpartum hemorrhage (all causes, over 500 c.c.)	2.45	3.10
Placenta previa	0.00	0.59
Premature separation of placenta	1.07	1.29
Retained placenta	1.9	0.43
Prolapsed cord	0.00	0.52
Multiple pregnancy	6.3	1.25
Brow presentation	0.4	0.17
Transverse lie	0.4	0.30

Table V summarizes the incidence of the complications of labor in the present series and contrasts them with the over-all incidence at the Sloane Hospital for Women from 1935 to 1952. It will be noted that prolonged labor and uterine inertia are not features of hydramnios as commonly stated in obstetrical textbooks. As a matter of fact, the incidence of prolonged labor and uterine inertia is lower in the present series than in the clinic population for the same period of time.

The third stage of labor was conducted by expressing the placenta as soon as there was evidence of placental separation. In 193 cases the duration of the third stage was from 1 to 30 minutes. In 5 cases the third stage lasted from 31 to 60 minutes. The third stage did not last over 60 minutes in any of the patients. There were 5 cases of postpartum hemorrhage due to different causes. Only one was due to atony of the uterus. There were 4 cases of adherent placenta that required manual removal. The total incidence of postpartum hemorrhage due to all causes was 2.45 per cent, and the incidence of retained placenta was 1.9 per cent. When compared to an incidence of postpartum hemorrhage of 3.11 per cent for the entire service, it appears that hydramnios does not predispose to this complication. We have not observed any increase in postpartum hemorrhage due to third-stage inertia.

There appears to be no basis for the statement that the incidence of transverse lie, prolapse of the cord, and premature separation of the placenta is more common in these than in normal cases.

Presentation and Type of Delivery.—

There were 198 cases in which the presentation was determined. Among the single pregnancies there were 91 per cent vertex, 7.3 per cent breech, 0.56 per cent face presentations and 0.4 per cent transverse lies. Among the twin pregnancies there were 23 vertex and 3 breech presentations.

The types of delivery differed from the average only in that there were about twice as many breech deliveries and the fact that there was a cesarean section rate of 8.8 per cent in contrast to the 6.8 per cent over-all rate. The reason for the higher section rate is not apparent from the analyzed data.

Fetal Mortality.—

Two hundred and nineteen babies were delivered from a total of 204 patients. Table VI shows the incidence of stillbirths and neonatal deaths in all the cases, divided according to the severity of the hydramnios.

TABLE VI. FETAL OUTCOME ACCORDING TO SEVERITY OF HYDRAMNIOS

TYPE OF CASE	NEONATAL DEATHS	STILLBIRTHS	LIVING AND WELL	
Severe cases (58 total)	12	42	11	(17%)
Moderately severe (76 total)	15	16	49	(61%)
Mild cases (70 total)	6	5	63	(85%)
Total	33	63	123	
Uncorrected fetal mortality		43.8%		
Corrected fetal mortality		36.5%*		

*Eliminating babies who weighed under 1,000 grams.

There were a total of 63 stillbirths and 33 neonatal deaths, an over-all uncorrected fetal mortality of 43.8 per cent. Of the 96 infants who died, 16 were previable (under 1,000 grams), 60 weighed between 1,000 and 2,500 grams, and 20 weighed over 2,500 grams. The corrected mortality for the total group was 36.5 per cent. It becomes immediately apparent from Table VI that there is a very close correlation between the severity of the hydramnios and the fetal outcome. An analysis of the causes of death of these babies showed that 46 died of congenital anomalies (57.5 per cent), 20 died of unknown causes (25 per cent), 9 died of obstetrical complications (11.2 per cent), and 5 died of prematurity (6.2 per cent). Among the obstetrical complications may be listed one cord complication, one unexplained case of fetal anoxia, one case of erythroblastosis, one breech extraction, one version and breech extraction, and one high forceps delivery. The last three babies died of intracranial hemorrhage. Complete autopsies were performed on 75 babies, giving an autopsy rate of 78 per cent. In about 20 per cent more, complete autopsies were not done, the specimen consisting mainly of external malformations, the fetus being preserved for teaching purposes. Table VII shows the number and percentage of the different congenital anomalies found in these cases.

The incidence of anomalies and pathological findings in the entire series of 204 cases is shown in Table VIII.

Spina bifida and meningocele are often given as the most frequent anomalies. This series shows that anencephaly and gastrointestinal anomalies were the most frequent. An important point to be observed is the incidence of gastrointestinal anomalies found in these cases. The most common gastrointestinal anomaly was diaphragmatic hernia, which occurred in 7 of a total of 20 cases of congenital gastrointestinal anomalies. Two infants had congenital bands with obstruction across the duodenum, 2 had malrotation of the

duodenum and intestines. There were 2 cases each of tracheoesophageal fistula, atresia of the esophagus and unattached mesentery, and there was one case each of stenosis of the duodenum, congenital intestinal fistula, atresia of the small intestine, internal intestinal hernia, and undescended small bowel. There were a total of 26 lesions in the gastrointestinal tract of which 21 (80.7 per cent) were obstructive or potentially obstructive lesions. The importance of these figures lies in the fact that many of them can be surgically corrected. The gastrointestinal anomalies are second in importance only to anencephaly. They should be looked for in every case. Prompt recognition would undoubtedly salvage many of these infants by prompt surgical intervention.

TABLE VII. CONGENITAL ANOMALIES AMONG 96 STILLBIRTHS AND NEONATAL DEATHS

ANOMALIES	NO. OF CASES	%
1. Anencephaly	27	28.1
2. Gastrointestinal	13	13.5
3. Diaphragmatic hernia	7	7.2
4. Umbilical hernia	1	1.0
5. Spina bifida	7	7.2
6. Cardiac anomalies	9	7.2
7. Microcephaly	3	3.1
8. Microphthalmus	1	1.0
9. Meningocele	4	3.1
10. Hydrocephalus	3	3.1
11. Malformation of genitourinary tract	1	1.0
12. Myelodysplasia	1	1.0
13. Chondrodystrophy	2	2.05

TABLE VIII. INCIDENCE OF PATHOLOGIC ABNORMALITIES AND CONGENITAL ANOMALIES IN ENTIRE GROUP

CONGENITAL ANOMALIES	%	PATHOLOGIC ABNORMALITIES	%
Anencephaly	13.2	Prematurity	21.0
Gastrointestinal anomalies	6.3	Maceration	12.2
Diaphragmatic hernia	3.4	Congenital atelectasis	5.4
Cardiac anomalies	4.4	Intracranial hemorrhage	4.4
Spina bifida	3.4	Aspiration pneumonia	1.4
Meningocele	2.4	Erythroblastosis	0.9
Microcephaly	1.8	Hyaline membrane pneumonia	0.9
Hydrocephalus	1.8		
Microphthalmus	0.4		
Malformation of genitourinary system	0.4		
Chondrodystrophy	0.9		
Myelodysplasia	0.4		

Summary and Conclusions

1. A review of 204 cases of hydramnios is presented, covering a period of 18 years at the Sloane Hospital for Women. The cases are analyzed with particular reference to prenatal factors, complications of labor and delivery, and fetal results.

2. The time of appearance of hydramnios bears a direct relationship to the ultimate severity of the disease. Similarly, the fetal outcome is in direct proportion to the severity of the condition, i.e., the more severe the case, the higher the fetal mortality.

3. The higher incidence of hypertensive toxemias and diabetes with hydramnios is corroborated in this study.

4. Labor and delivery result in no more obstetrical complications than in normal cases. In contrast to other reports, this series offers no evidence of any greater incidence of such complications as: (a) prolonged labor, (b) uterine inertia, (c) postpartum hemorrhage, (d) premature separation of the placenta, (e) prolapse of the cord, or (f) transverse lie.

5. Induction of labor in these patients is not a harmful procedure.

6. The incidence of breech presentation appears to be increased.

7. The main problem in hydramnios is not the obstetrical complications of labor and delivery, but the fetal mortality.

8. An analysis of the causes of the high fetal mortality is made. The high incidence of gastrointestinal anomalies and diaphragmatic hernias is noted. They rank second only to anencephaly as the most common defect. Spina bifida and meningocele, commonly stated as the most frequent congenital defects in these cases, were relatively uncommon.

9. A plea is made for more detailed study of these babies since many of the gastrointestinal anomalies can be treated surgically.

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ETIOLOGY OF CEREBRAL PALSY: AN EXPERIMENTAL APPROACH

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CURRENTLY, etiological factors in cerebral palsy are assumed to be related to constitution factors, maternal health during pregnancy, and associated intrauterine anoxia, anoxia during delivery, and sequelae of infectious diseases during infancy. When the diagnosis of cerebral palsy is made in a child, etiological factors must be assumed from the history. This procedure of "discovering" causes from the history sometimes fails to provide clues as to the etiology in a specific case. Clinically there are many cases with obvious signs of brain damage, but with histories that are noncontributory. On the other hand, it has been reported[2] that children who were known to have had difficult deliveries or have been anoxic at birth developed relatively normally. Thus it seems apparent that "causative factors" in cerebral palsy are in need of further clarification. This study is one attempt at such a clarification. The contribution of this study is to look forward temporally instead of backward, and after noting the child's actual behavior and symptoms at birth and neonatally, follow his progress through two and one-half years. In this way, the validity of certain "etiological" factors can be substantiated.

Materials and Method

The experimental procedure was as follows:

1. A detailed study of one hundred diagnosed cases of cerebral palsy* was undertaken, and the apparently significant factors in the history were isolated.[3] Of these, the following "significant findings" were selected for study: *obstetrical:* midforceps delivery, breech delivery, prolonged pregnancy, prolonged labor; *neonatal:* prematurity, oxygen required, transfusions required, cyanosis, hypertonicity, and listlessness. These findings, where computable, were statistically of a significantly greater incidence in the histories of 100 cerebral palsied children than in the histories of 504 cases, consecutive ward births at the Providence Lying-In Hospital in 1949. This hospital's admission rate is one of the highest in the country, and its maternal and neonatal death record is one of the smallest in the country. The period of selection was during the postwar period when a high standard of medical and nursing care was available.

2. Utilizing the "significant findings" previously listed as presumptive causes of brain damage, all the infants in the group of 504 whose hospital histories indicated clearly any one of them were chosen for study. There were 36 infants whose histories (prenatal, obstetrical, or neonatal) contained one or more of the previously mentioned "significant findings." Each of these infants was carefully followed by Providence District Nurses every three

*Cerebral palsy as defined in this study consists of aberrant neuromotor signs resulting from brain damage with or without other associated findings such as convulsions, mental retardation, and behavioral disorders.

months for a period of two and one-half years. Of this group of 36, two and one-half years later it was possible to study completely only fifteen cases (41 per cent of the group), since many families had moved out of the state. This study is therefore based on 15 children who had one or more "significant findings" at birth. This group will be designated the "suspicious" group. The relatively small number of children in the study is advantageous in that this small group could be studied individually, intensively, and as completely as possible with a wide variety of testing instruments and conditions, rather than more superficially and in a less detailed fashion than would have been possible with a larger group. The small size of the sample studied does not negate the statistical significance of the differences that were found.

3. A random sample of 17 children was obtained from the population of 504 infants. These 17 were closely matched with the 15 for sex, date of birth, and socioeconomic status. The only way they varied from the 15 "suspicious" cases (previously described) was by absence of any "significant finding" in their histories. These were, by all clinical criteria, normally healthy infants at birth. These children, designated the "control" group, were studied in identical fashion with the "suspicious" group.

The suspicious and control histories were compared with 20 children with cerebral palsy also born at the Providence Lying-In Hospital during the post-war period. The detailed comparisons are presented in Table I. It should be noted that the control mothers had more pregnancies, but had significantly fewer stillbirths than either the "suspicious" or cerebral palsy cases. An inspection of this table shows that, of the vast amount of information compared, there are no other outstanding differences between the two groups.

4. At the end of two and one-half years, both groups of children (15 "suspicious" cases and 17 healthy-at-birth controls) were evaluated as follows:

a. A complete physical examination was given.

b. A complete neurological examination was given.

c. A psychological examination was given utilizing the Merrill-Palmer Scale of Mental Tests as the testing instrument.

d. Vineland Social Maturity Scale was completed in an interview with the parents (usually the mother).

e. Parents were requested to disclose any complaints, symptoms, or difficulties observed in their child at the current time of the examination.

Results

"Suspicious" Cases.—

Results of the follow-up studies of the "suspicious" cases two and one-half years later are summarized in Table II. As stated before, all the children in this group had positive birth and neonatal findings. This was the criterion for selection of this group.

Of the 15, 4 (27 per cent) of the children had a combination of abnormal physical, neurological, psychological, and/or social findings upon examination. All 4 were retarted mentally (I.Q. below 80) and each had some suspicious abnormal physical finding; 2 had difficulty in locomotion or balance; 2 had behavioral disorders. These findings are graphically shown in Fig. 1.

Although 5 other children had some slight deviation in development, the delays were minimal, and in at least 3 cases seemed due to environmental factors rather than organic brain damage.

A thorough analysis of the histories of the 4 children in the "suspicious" group who were notably retarded and physically deviant revealed one factor

TABLE I. DETAILED HISTORY OF PATIENTS STUDIED IN SUSPICIOUS AND CONTROL GROUPS (COMPARISON OF CEREBRAL PALSIED PATIENTS BORN 1945)

ITEMS INVESTIGATED	SUSPICIOUS		CONTROL		CEREBRAL PALSY	
	Total = 15		Total = 20		Total = 20	
Family History.—						
Mental or neurological abnormalities	0		0		0	
Maternal History.—						
Previous pregnancies	20		41		38	
Alive	16	80%	38	91%	31	81%
Stillborn	4	20%	3	9%	7	19%
Age						
15-25	11	71%	12	60%	10	50%
26-35	2	14%	6	28%	8	40%
36	2	14%	2	10%	2	10%
Race						
White	11		16		18	
Negro	4		4		2	
Previous disease of mother						
Diabetes	0		0		1	
Tuberculosis	1		3		2	
Kidney disease	2		3		0	
Other	15		28		4	
Previous transfusions	0		1		0	
Present Pregnancy.—						
Nausea	7	53%	11	55%	9	52%
Vomiting	8	57%	11	55%	7	44%
Gastrointestinal disturbances	3		8		6	
Vertigo	2		7		2	
Headache	7		8		5	
Edema	4		5		6	
Vaginal bleeding	2		5		1	
Physical examination						
Pelvic type: gynecoid	12	85%	15	94%	14	70%
Pelvic type: anthropoid	2	15%	1	6%	4	20%
Blood studies*						
Hemoglobin						
Less than 10 Gm.	1		9		1	
10-14 Gm.	13		10		5	
Rh Negative	4	30%	1	5%	2	11%
Labor.—						
Analgesia						
Seconal, 3 grains	4		2		5	
Demerol, 100 mg.	0		2		0	
Nembutal, 3 grains	1		0		1	
Scopolamine, 1/100 Gm.	0		0		4	
Progress during labor						
Bleeding	0		0		2	
Blood pressure, abnormal	0		0		2	
Membrane rupture	4	28%	7	39%	7	39%
Onset of labor						
Spontaneous	15	100%	20	100%	16	80%
Induced	0		0		1	
Surgical	0		0		3	

TABLE I—CONT'D

ITEMS INVESTIGATED	SUSPICIOUS		CONTROL		CEREBRAL PALSY	
First stage						
Duration						
0-5 hours	4		3		4	
6-15 hours	8		12		14	
16-24 hours	1		2		4	
Over 24 hours	1		1		2	
Second stage						
1-12 min.	4		3		4	
16-30 min.	3		8		7	
31-60 min.	4		4		4	
60+	2		2		5	
Contractions, character						
Poor	1		1		2	
Irregular frequency	0		1		1	
Termination of labor						
Spontaneous	10		18		12	
Operative						
Low forceps	1		1		9	
Midforceps	3		0		2	
Forceps to the aftercoming head	1		0		1	
Cesarean section	1		1		3	
Position						
Vertex						
ROA	7		6		4	
LOA	4		14		9	
LOP-LOA	2		0		2	
ROT-ROA	1		0		1	
Double footling	1		0		0	
Breech	0		0		4	
Anesthesia						
Gas, oxygen, ether	9		11		18	
Gas, oxygen	3		6		2	
None	1		0		0	
Total duration of labor						
1-5 hours	3		2		3	
6-15 hours	8		12		10	
16-24 hours	0		3		5	
24 hours	3		1		2	
Third stage						
Placental abnormality	0		0		6	
Infant.—						
Premature	2		1		3	
Abnormalities of cord	4		2		4	
Asphyxia treated	2		0		6	
Prolonged pregnancy	1		0			
Caput succedaneum	4		3			
Total injuries or abnormilities at birth	13	87%	2	5%	10	50%
Cyanosis	1				6	
Hydrocephalus	1					
Linear skull fracture	1					
Cyanosis, secondary to cord around neck	1		2			
Cyanosis, cause unknown	2					

TABLE I—CONT'D

ITEMS INVESTIGATED	SUSPICIOUS		CONTROL		CEREBRAL PALSY
Forceps bruise right	1				
Fractured right clavicle	1				
Abnormal placenta	1				
Brachial palsy	1				
Bleeding from cord	1				
Neonatal Progress.—					
Normal	7	45%	20	100%	
Hypertonicity (including convulsions)	3		0		
Hypotonicity (listless)	3		0		
Feeding difficulties	1		0		
Cyanosis	1		0		
Developmental Progress.—					
Abnormal					
Head control	2		2		
Sit alone	2		1		
Stand alone	1		1		
Walk alone	2		0		
Sentences	6		3		
Psychological:					
I.Q. below 70	2		1		

*Serological studies for syphilis were negative in all groups.

TABLE II. SUSPICIOUS SIGNS OR SYMPTOMS AT BIRTH (15 CASES)

CASE NO.	SEX	PREVIOUS HISTORY			PRESENT STATUS (AGE 2½)				REMARKS (AGE 2½)
		MATERNAL	BIRTH	NEONATAL	PHYSICAL	NEUROLOGIC	PSYCHOLOGIC	SOCIAL	
1	F					Abnormal			Listless, apathetic, strabismus
2	M		Abnormal			Abnormal			Mental retardation with delayed development
3	M		Abnormal		Abnormal		Abnormal		Mental retardation, speech delay, distractibility
4	F	Primipara	Abnormal			Abnormal			Mental deficiency, ataxia
5	F		Abnormal					Abnormal	Retarded social development
6	M		Abnormal		Abnormal				Facial paralysis
7	M		Abnormal						Behavior problem
8, 13, 15	M		Abnormal						
9, 11	F		Abnormal						
10	F		Abnormal						Twin of Case 4
12	F		Abnormal						Hyperactive, sleep resistance
14	F		Abnormal						

TABLE III. CONTROL CASES, NO SUSPICIOUS SIGNS OR SYMPTOMS AT BIRTH (17 CASES)

CASE NO.	SEX	PRESENT STATUS (AGE 2½)				REMARKS (AGE 2½)
		PHYSICAL	NEUROLOGIC	PSYCHOLOGIC	SOCIAL	
1	F		Abnormal			Bilateral Babinski reflexes
2	F	Abnormal		Abnormal		Mental deficiency
3	F		Abnormal			Cerebral palsy, mental retardation
4	M	Abnormal				Cerebral palsy; spastic secondary to meningitis at age 2
5	F					Behavior problem
6		Abnormal				Heart murmur; moderate
7			Abnormal			Increased deep reflexes
8, 11, 13	M					
9, 10, 12, 14, 15, and 16	F					
17	M					Eating problem (slight anoxia at birth)

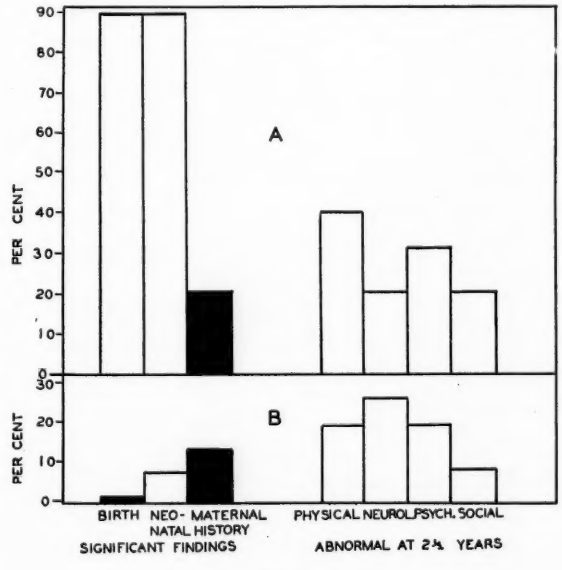

Fig. 1.

in the history in common: *three of the four mothers had had a previous abortion.* The mother of the fourth child was a primipara. In only one mother could a possible reason for her previous abortion be ascertained at the time of this study, and this was probably due to chronic renal disease. Only one mother had Rh-negative blood. No other mother in this group had had a previous abortion.

Control Cases.—

Of the control group who were chosen specifically for the absence of any abnormality during the birth or neonatal period, there was one possible case of cerebral palsy (abnormal neurological findings and mental retardation), one case with a positive Babinski reflex, and one other case of mental deficiency (Table III). In other words, 3 of 17, or 18 per cent, of the control group evidenced definite physical or mental abnormality at the end of two and one-half years, despite a healthy birth and neonatal history according to all observations and records. One child had a diagnosis of "cerebral palsy, spastic, right monoplegia" at the age of 2½ subsequent to meningitis at the age of 2 years.

Of the 3 cases in the control group with abnormal findings, the one factor in common was a previous abortion in the mother's history. No other mother in this group had had a previous abortion.

Comment

It seems striking that the one common finding in the abnormal cases of both the "suspicious" and control groups was the previous abortion in the mother's past history. It seems even more striking since abortion is also found to a high degree (28 per cent) in mothers of children already known to have cerebral palsy.[3] This finding agrees essentially with that of Lilienfeld and Parkhurst[4] who found that mothers of cerebral palsied children had approximately 35 per cent more infant loss in previous pregnancies than in the normal population. This is a significantly higher incidence than in the general population.[5] Therefore, it must be assumed that the mothers of these children have some constitutional factor or endocrine dysfunction which contributes to the aberrant development of their offspring.

Let us consider the relationship of prenatal factors to the subsequent development of cerebral palsy. One could postulate that this maternal "constitutional" factor (heredity, poor nutrition, physiological dysfunction) may in some way lower the threshold of resistance through intrauterine anoxia in the newborn so that he is more susceptible to brain damage than an infant born to a mother without this handicap. In our study, although all the cases of the "suspicious" group suffered some trauma at birth (based on hospital records, not parent histories), nevertheless, those whose mothers had not previously aborted seemed to develop normally. On the other hand, the infants who were subjected to birth trauma *and* who were born of mothers with a history of previous abortions or miscarriages were later found to be more developmentally handicapped. Baumgartner's[6] recent statistical survey of infant and neonatal mortality supports our hypothesis that there is a distinct relationship between neonatal death and mothers who were subject to previous miscarriage.

There may also be some connection between our results and those of Ingalls[7] who demonstrated in mice that abortions or malformations of the offspring could be produced by subjecting the pregnant females to varying degrees of anoxia. It may well be that acute anoxia at birth is not as important as previously considered. Rather, long-standing intrauterine anoxia may be more significant in the etiology of brain damage.

In other words, this study seems to show conclusively that birth trauma *alone* is not necessarily responsible for later evidence of brain damage. One aspect of prevention of cerebral palsy perhaps lies in greater emphasis in research on maternal reproduction physiology, particularly in those mothers who are subject to abortions.

Summary

1. A study of possible causative factors in cerebral palsy was made with 15 children who had "suspicious" findings of brain damage at birth and neonatally, and 17 healthy controls selected as a random sample from 504 consecutive ward births.

2. Only 4 (27 per cent) of the "suspicious" group had abnormalities in physical, psychological, and/or social development when intensively studied after two and one-half years. Three (18 per cent) of the control group had similar findings.

3. The only factor common to the deviantly developed children in *both* groups was a history of previous abortion in the mother.

4. It is concluded that one important area of research in the etiology of cerebral palsy involves further investigation of reproductive physiology.

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INFECTIOUS HEPATITIS AND PREGNANCY*

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OUR thinking on infectious hepatitis has undergone considerable change in the past ten years. The first suggestion in the literature that the condition was infectious dates back to 1923 when two interns in Sweden[1] noted that an epidemic of jaundice in a diabetic ward subsided when the blood-counting lancet was sterilized between patients. There was no further mention of the etiology until Roholm and Iverson[2] in 1939 announced that acute yellow atrophy of pregnancy was an infectious disease. The literature to date has been only a verification of their observations. The findings in both the epidemic and isolated forms of infectious hepatitis have demonstrated a common etiology and also the fact that infectious hepatitis and homologous serum jaundice are identical pathologically.

In 1947 Zondek[3] reported from Palestine an epidemic of viral hepatitis involving 29 pregnant women. In 12 of his 29 cases in pregnancy a definite contact was established. The incubation period varied from 8 to 42 days. Although the epidemic was relatively benign, cases that ended fatally occurred exclusively in pregnant women. Approximately 62 per cent of Zondek's patients were definitely undernourished with a negative protein balance. All patients showed a vitamin B deficiency. In severe cases he noted that there was a drop in blood urea levels. Although the blood cholesterol was usually decreased with depression of the ester fraction, in the patient who died he found no depression of cholesterol levels. Premature labor initiated the fatal phase in his 5 patients who died. The labors were relatively easy. In 2 cases severe uterine hemorrhage occurred when hepatic coma set in. Three of the patients who recovered became pregnant again and had no complications. In 2 cases chronic hepatitis was a sequel. The babies showed no evidence of the hepatitis. Zondek recommended a high-protein, carbohydrate, vitamin diet and the avoidance of operative intervention.

Dill[4] reviewed hepatitis in pregnancy in 1950. His conclusions agree with those of Zondek that the disease is infectious and he found that the disease in the third trimester is invariably fatal. He states that the incidence of hepatitis in pregnancy varies between 1:2,000 to 1:20,000 cases. The over-all incidence of hepatitis in the population is approximately 4 per cent. He elicited as the prodromal symptoms anorexia, fatigue, nausea, vomiting, and mild intestinal disturbances. He felt that therapy was of little value because the diagnosis is made late in the course of the disease. His six cases ended fatally. Mickal[5] reporting from the Charity Hospital in New Orleans, added 15 cases occurring in pregnancy. Two patients were in the third trimester and had a fatal outcome.

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Roth[6] reported 4 cases from the U. S. Naval Hospital in Chelsea, Massachusetts, and concluded that the maternal mortality was no different from that in the nonpregnant woman.

Farquhar and associates[7] reported phenomenal recovery using Aureomycin as treatment in 2 patients who had developed coma.

We wish to report 9 cases of hepatitis in pregnancy with a review of the symptomatology and the objective findings. We are indebted to Dr. Richard Capps[8] of St. Luke's Hospital, Chicago, for 3 cases in this series.

Our series includes 1 case in the first trimester, 3 cases in the second trimester, and 5 cases in the third trimester. The prodromal symptoms presented themselves anywhere from 2 to 21 days prior to the onset of noticeable icterus, the average time being 10 days. General malaise and fatigue were exhibited by 5 of our patients. Four patients were first seen for chills and fever. Three showed vague bowel dysfunction associated with three to five bowel movements a day. Three patients had anorexia and 2 complained of nausea and vomiting. Only one patient in our series was admitted prior to the onset of jaundice, persistent nausea and vomiting being her chief complaints. All of the others were sent to the hospital after clinical jaundice was first detected.

A source of contact was looked for in each of the cases. A positive source of contact is difficult to establish, but we found that 4 patients had a possible source of exposure. The contact was either from blood-counting lancets or from hypodermic-needle puncture. One of the patients had a questionable contamination when she received gamma globulin. In 4 cases no obvious source of contact was established. The probable incubation period varied between 21 and 58 days.

The course of the active phase of the disease in our cases has been divided into the acute, the chronic, and the fatal cases. The length of the active phase of the disease has been between two weeks and four weeks.

The 6 patients who had the acute form of the disease were studied as to duration of pregnancy and as to severity of the disease.

The patient who developed the disease in the first trimester had a mild case and showed satisfactory recovery within two weeks. She subsequently delivered a full-term normal infant with no complications.

Three patients with the acute form were in the second trimester. One of them delivered a normal infant four months following her infection and had no complications. Another delivered approximately fourteen weeks following her attack and gave no indication of any hepatic damage. The third patient recovered from her infection, delivered a normal baby and shows no evidence of the disease.

The acute cases in the third trimester proved to be the most severe ones. The first of these patients developed the disease in the thirty-second week and it reached its peak about two weeks later. She was in the healing phase or past the crisis when she delivered three weeks prematurely. The infant was in good condition. The patient's convalescence was uneventful. She has subsequently had another normal pregnancy and delivery. The second patient in this group was a 24-year-old primipara who developed hepatitis near the end of the seventh month and delivered a normal premature infant in the eighth month. She had an uneventful recovery and delivered another baby one year later with no ill effects or recurrence. The third patient in this group was admitted one week after the onset of the prodromal signs. Jaundice was apparent on her admission. Two days following her admission she had a marked diuresis of 5,000 c.c. of urine. Capps has described this as an encouraging sign of beginning recovery and has coined the phrase "hepatic crisis." Four days following the diuresis she delivered prematurely an eight months' infant that died in the neonatal period. The evening of delivery she went into a

TABLE I. LABORATORY DATA

	MRS. C.—WEEK OF PREGNANCY					MRS. PR.—WEEK OF PREGNANCY		MRS. M.—WEEK OF PREGNANCY							MRS. PL.—WEEK OF PREGNANCY			MRS. S.—WEEK OF PREGNANCY		MRS. PK.—WEEK OF PREGNANCY		
	32	33	34	37	38	16	17	20	21	22	31	36	39	40	29	30	31	12	13	31	32	33
Hemoglobin (Gm.)	9		11	10		11		10		10½	9	11	12	10	14	14		11		12		
Erythrocyte count (millions)	3.3		3.6	3.1		3.6		3.4		3.4	3.4	3.7	4.7	3.8	3.2		3.3	3.4		3.8		
Icterus index	18	23	11	6		35									85	50	18			29		
Protein (Gm. %)	5.7		6.4			6.6	6.5				7.8				6.3	6.6		6.5		5.4		4.7
Albumin	3		3.6			3	3				3.5				3.3	3.9		4.3		4.6		
Globulin	2.6		2.8			3.5	3.5				3.6				3.0	2.7		22		1.8		
Alkaline phosphatase	13	18½	22	16	11		18	14	4.5	14	17	28½	34½	35				6	5	12		
Bilirubin test	3.5	5.3	1.3	16.1	11	12		6	7	8½	2	2½	2½	2½				2½	2	13	10	21
Prothrombin	77					60		76	60	74			72	78				70		46	13	
Hanger test	4+											–		–		–		–	–	4+	4+	

stupor, the jaundice deepened, and she went into mild hepatic coma. Two days later she became brighter and on the fourth day she excreted 8,000 c.c. of urine and recovery was quite rapid. The delivery in this case probably caused an exacerbation in the healing liver and caused a recurrence of the process.

The one case of chronic hepatitis developed in the twentieth week and the patient delivered a premature infant in the thirty-seventh week of gestation. She is six months post partum now and still has evidence of hepatic damage. Her labor and immediate postpartum period were complicated by a lowered prothrombin time (32 per cent). She had an abscessed tooth pulled in the eighth month with postoperative hemorrhage and following delivery she developed a large hematoma extending from the episiotomy into the vulva. This area was evacuated and packed, but bleeding recurred the following day. This is the only chronic case in our series.

The last 2 cases were the ones in the third trimester which ended fatally. The first patient was a 35-year-old multigravida who contracted the infection in the eighth month. She had diarrhea for approximately three weeks followed by jaundice. She was given ACTH on admission for three days and became anuric shortly after admission with an icteric index of 90 and a nonprotein nitrogen of 64 mg. per cent. The prothrombin time was practically nil. She went into labor four weeks prematurely and delivered a normal infant that died shortly after delivery. Hepatic insufficiency increased progressively and the patient died approximately eighteen days post partum.

The second fatal case was that of a 23-year-old primipara who was underweight and had gained only 8 pounds throughout pregnancy. Near the beginning of the third trimester she developed bronchopneumonia following an early bronchiectasis and had almost intractable hyperemesis. She appeared to recover, but was seen three weeks later with early jaundice. Three days after admission she went into labor and delivered a normal thirty-six weeks' infant that died in six hours. The patient went into a rapid hepatic insufficiency and died in hepatic coma one week later.

The autopsy findings were similar in these two cases. The livers were small and microscopically characterized by a massive periportal necrosis with areas of inflammatory reaction. Early fibrosis was evident as were varying degrees of regeneration of the liver cells. Hepatitis, eclampsia, and chemical liver necrosis are identical pathologically. It is impossible to differentiate the sections microscopically.

The laboratory diagnosis in our series showed an elevation in the icteric index, alkaline phosphatase, total bilirubin, cephalin flocculation, thymol turbidity, and cephalin cholesterol flocculation. The nonprotein nitrogen was elevated in only the 3 patients who had coma. The prothrombin was depressed in all cases. The total serum protein was depressed only in the terminal cases. The blood counts were not remarkable. Capps had recently done liver function tests on forty normal pregnant women as well as on the newborn babies. In all but three of his patients he found that the alkaline phosphatase was normally elevated and the total bilirubin slightly elevated. In a recent epidemic of infectious hepatitis he found that abnormalities in total bilirubin were not consistent enough to be of any diagnostic value. He concluded that the three tests of merit in the pregnant woman were cephalin flocculation, thymol turbidity, and zinc sulfate turbidity. Table I reviews the laboratory data.

The treatment of infectious hepatitis in pregancy is a twofold problem, both medical and obstetrical. An internist well acquainted with the treatment

of hepatic insufficiency and a conservative obstetrician are the best combination. The first approach to treatment should be preventive. Treament of the disease in the first two trimesters is mainly directed at the hepatitis. General supportive measures such as a high-vitamin, high-carbohydrate, and high-protein diet are essential. Fortunately, the prognosis is favorable in the first two trimesters. It is in the last trimester that the problem becomes acute, for it is then that we are faced with the double-barreled problem of progressive hepatic damage made worse by the stress and strain of maturing pregnancy. The question of what to do in the seriously ill patient arises: whether to effect delivery or not. When massive necrosis of the liver occurs premature labor usually ensues. Any abdominal operative procedure is contraindicated for, as in other cases of severe liver disease, this usually ends in a fatal outcome. As our most severe cases in this series show, the disease is more serious in the postpartum period. Whether this is caused by the load of detoxifying the estrogens and involutionary proteins or not is a question unanswered, but it does show us that emptying the uterus does not solve the problem. So far as the pregnancy is concerned, treatment should be directed at the disease itself. If premature labor does ensue, preparations should be made for the control of hemorrhage. As safe an analgesic and anesthetic agent as possible should be administered. The problem of whether to give blood or not prior to delivery for the improvement of the clotting mechanism is unanswered. One dislikes to gamble on an adverse blood reaction in an already damaged organ. The two cases that we have presented in which blood was given had a minimal blood loss during delivery. The other patient with a lowered prothrombin time received no blood and developed a severe hematoma which necessitated two units of blood. The use of aureomycin seems indicated because of the few successful reports in the literature. Its effectiveness is far from proved. The postpartum period is largely a medical problem based on supportive therapy and the maintenance of an adequate fluid and electrolyte balance. A substantial caloric intake is imperative.

From our own experiences and a review of the literature we have arrived at the following conclusions:

1. Hepatitis is an infectious disease dangerously complicating pregnancy.
2. Patients who have hepatitis in the first two trimesters of pregnancy may recover or the disease may become chronic.
3. Hepatitis in the third trimester and postpartum period is a serious complication with a high mortality rate.
4. Since the disease is usually well advanced before a diagnosis is made, treatment is mainly prophylactic with general supportive measures.
5. Conservatism in the handling of the pregnancy is recommended.

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Discussion

DR. ROBERT M. KARK (By invitation).—I will say that during the past year I have been much distressed by having patients die from infectious hepatitis while I was caring for them. I have been unfortunate in seeing 6 young women in the third trimester of pregnancy become jaundiced and die.

The common causes of infectious hepatitis are two viruses. Virus A which causes so-called catarrhal jaundice or infectious hepatitis is passed by fecal contact. So-called homologous serum hepatitis is caused by Virus B or SH Virus and is passed by needle or transfusion. There are many other infectious diseases which cause hepatitis. For example in the Research and Educational Hospital of the University of Illinois, there is a pregnant woman in the third trimester who has jaundice as a result of leptospiral fever, a rare cause of hepatitis.

Viral hepatitis is a mild disease in the general population, but it seems to be rather dangerous in women after the menopause as well as in the third trimester of pregnancy.

At the beginning of World War II, physicians began to recognize that they were seeing a new type of hepatitis which was being passed to soldiers by inoculation and during transfusion. This was so-called homologous serum hepatitis, which is a poor name, as other types of hepatitis can also be passed by transfusion of blood and blood products. Virus B or SH hepatitis is passed from person to person by transfusion and by needle punctures. The virus cannot be killed except by heat, and it is long lived in the blood stream. There was an unfortunate incident in Scotland some five years ago when a physician decided to do skin tests with ascitic fluid from a patient who had had jaundice thirty years before. Sixty-five individuals were given minute intradermal injections of the fluid. All developed jaundice, and six of them, including a young physician, died. I tell you this story because I am sure that obstetricians, like physicians and surgeons, are sometimes guilty of passing on serum hepatitis, through the use of improperly sterilized needles. Serum hepatitis is a preventable disease, and we must do everything we can to make sure that the blood and blood products we use are not contaminated with the virus. The paper by Flaum clearly indicates that serum hepatitis is transmitted by use of improperly sterilized needles. Dr. Long has told you about this, and I will not labor the point any further.

Virus A, infectious hepatitis, which we used to call catarrhal jaundice, is spread from man to man by fecal contact, and its appearance is associated with poor hygiene. I have a mother in the ward now who is pregnant the third time, and I am sure she got infectious hepatitis from her child. I am certain she was careless in handling the child's clothes and did not wash her hands before she took her meals and passed the infection from her child's clothes to herself. We also see a number of people around the hospital who get infectious hepatitis. It is not at all uncommon among residents and nurses. The reason, I think, is clear. So many of us have got to the point where we now stop washing our hands after seeing patients. Everybody feels that antibiotics are the answer to all infections so we have stopped doing what I was taught to do in the preantibiotic days—we have stopped scrubbing our hands before and after seeing patients and before eating our meals. I believe that it is most important as a part of prenatal training to teach mothers to wash their hands thoroughly after handling their children's clothes and to wash their hands very carefully before each meal.

Virus A hepatitis is very much like poliomyelitis. It is common in children in areas of poor hygiene and attacks adults in areas of good hygiene. The whole world is covered by a thin layer of feces which is thicker in Egypt and other Eastern countries where children get infectious hepatitis. The layer is thin in the United States and in Scandinavia where adult infectious hepatitis has become quite a problem recently.

With regard to therapy, the damage is done when a patient comes down with jaundice. We follow the course of the disease by the use of three tests: serum cholinesterase, the thymol flocculation test, and gamma globulin levels. We offer the patient vigorous supportive measures. These consist of bed rest, and a high-protein, high-caloric dietary regimen which the patient must be made to take even though the appetite is poor. If the patient will not eat, the food must be given by tube. It is most important for the doctor to know exactly how much his patient has eaten at each meal and this means he must cooperate closely with the dietary department of the hospital. When such patients go into coma, tube feeding and concentrated intravenous glucose solutions are the only answer to a nasty situation.

DR. LONG (Closing).—There has been considerable interest in regard to the effect of the hepatitis on the fetus. This is of two types: (1) the effect of a virus infection in the first trimester with resulting fetal deformity, and (2) the transfer of the infection to the baby. Reports are coming in on the abnormalities in the fetus. The infection in the newborn, however, is extremely rare.

RUPTURED INTRACRANIAL ANEURYSM DURING PREGNANCY: DIAGNOSIS AND TREATMENT

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WHEN the alarming signs and symptoms of subarachnoid hemorrhage occur in a pregnant patient, a cerebral complication of toxemia is usually suspected. Most nonobstetrical reports claim the rupture of an intracranial aneurysm to be the commonest cause of subarachnoid hemorrhage.[1, 2, 3] Schreiber,[4] reporting from the Harper Hospital in Detroit, claims that, in hospitals where this condition is carefully sought for, the incidence of one case per month is not unusual. Contrarily, it is considered to be a rare complication of pregnancy and is neglected completely by most textbooks of obstetrics. Hamby[5] in his monograph, "Intracranial Aneurysms," makes no mention of it as a complication of pregnancy. A review of the literature reveals only two cases proved by carotid angiography.[6, 7] In the remaining reports the diagnosis is only assumed on the basis of the symptoms and cerebrospinal fluid or is made at necropsy. It is the purpose of this paper to clarify the differential diagnosis, review the literature, and discuss the treatment according to physiological principles.

Etiology

There are three types of intracranial aneurysms generally described: (1) congenital, (2) mycotic, and (3) arteriosclerotic. Chief interest is centered on the congenital, which is saccular and occurs in the region of the angles formed by the bifurcation of the arteries of the circle of Willis or their branches. Common synonyms used are congenital, developmental, bifurcation, and berry aneurysms. Bremer[8] showed embryologically that the defects in the media at the bifurcations of the circle of Willis are true congenital aneurysms, an origin different from those previously postulated in the theories of Glynn[9] and Richardson and Hyland.[2]

Signs and Symptoms

Congenital aneurysms of the circle of Willis usually show few signs or symptoms until they rupture. Sudden headache is the most common primary symptom, usually occipital, then generalized. This most frequently occurs during ordinary activity. Other early signs are nausea, vomiting, and nuchal rigidity, followed in different cases by hemiplegia, weakness, convulsions, numbness, vertigo, unconsciousness, and visual disturbances. The temperature may be elevated and bradycardia is often present due to increased intracranial pressure. The symptoms vary with the degree of hemorrhage. Death often occurs without warning. The ocular signs in aneurysms of the circle

of Willis have received a great deal of attention.[10] Eye pain associated with ptosis and dilatation of the ipsilateral pupil should lead to a suspicion of an aneurysm of the anterior portion of the circle of Willis.

Grossly bloody spinal fluid is diagnostic of a hemorrhage which has either originated in the meninges or extended from the brain into the ventricles or subarachnoid space. A spinal puncture during the acute stage usually shows an elevated pressure. Other conditions to be ruled out are hypertensive cardiovascular disease, epilepsy, brain tumors, meningitis, multiple sclerosis, traumatic intracranial hemorrhage, cerebral embolism from foci such as rheumatic carditis and cerebral thrombophlebitis, leukemia, hemophilia, and other blood dyscrasias. The history of a previous aneurysm or similar symptoms must make one suspicious of another rupture. Toxemia is ruled out by the absence of its classical triad. The diagnosis was formerly made, before the advent of carotid angiography, on the basis of a history, physical findings, and examination of the spinal fluid. This is not enough to establish a positive diagnosis, however, as exemplified by the case reported by Lerer,[11] whose patient, in the fifth month of pregnancy, suddenly experienced all the signs and symptoms associated with rupture of an aneurysm of the circle of Willis, but at postmortem no evidence of a congenital aneurysm was found. Most of the early reports of intracranial hemorrhage during pregnancy have no angiography or postmortem results,[12-19] leaving the ultimate lesion in doubt.

Cerebral angiography introduced by Moniz[20] in 1927 and fully reported in 1934, stimulated an interest in intracranial aneurysms and vascular malformations. Gross[21] in 1939 introduced the use of Diodrast for the demonstration of the cerebral circulation radiologically.

Prognosis

Subarachnoid hemorrhage due to the rupture of an intracranial aneurysm is associated with a high mortality, even without the added factors introduced by pregnancy and labor. According to Rhoads,[22] about 50 per cent of the cases of ruptured intracranial aneurysm end fatally. Of those who recover on conservative therapy, a large number die during the ensuing year as a result of a second hemorrhage. Schreiber[4] claims that one-third of his patients died during the first admission, and, of those surviving the first week, one-half had recurrences.

Treatment

The obstetrician or surgeon who is suddenly confronted with such a problem is often at a loss as to the best method of management. The treatment of subarachnoid bleeding due to rupture of an intracranial aneurysm is still a matter of controversy. Some physicians belong to the "do nothing" school and treat their patients with expectant optimism, hoping that the tear in the aneurysm will become sealed with a clot and that the bleeding will stop. Unfortunately, this is not usually the case.

It seems to us that sound physical and physiological principles dictate that the first consideration is to control intracranial bleeding. It is now fairly well established that most aneurysms of the intracranial portion of the internal carotid artery and of the proximal branches of the circle of Willis can be successfully treated by ligation of the common or internal carotid artery in the neck.

Historical

John Abernathy,[23] John Hunter's immediate successor in London, ligated the common carotid artery for hemorrhage in 1798, but his patient died 30 hours later. Fleming in 1803,[24] a young surgeon in the Royal Navy, is credited with the first successful ligation of the common carotid artery. His patient attempted to commit suicide by cutting his throat while serving on

H.M.S. Tonnant. Fleming treated the neck wound and his patient was convalescing satisfactorily when eight days later, during a severe paroxysm of coughing, the carotid artery burst. Fleming cut down on the common carotid artery below the wound and tied it. The patient made an uneventful recovery. During the first half of the nineteenth century, ligation of the carotid artery was frequent, not only for hemorrhage and peripheral aneurysms but also for epilepsy, psychosis, and trigeminal neuralgia. In 1902, Horsley[25] ligated the right common carotid artery in the neck for an intracranial aneurysm discovered during a craniotomy for a suspected brain tumor. His patient was followed for five years and was well at that time. Sporadic cases of carotid ligation for intracranial aneurysm appeared in the literature from then until 1940 when Schorstein[26] reported 60 cases of carotid ligation for intracranial aneurysms of spontaneous origin. Rogers[27] in 1947 reported ligation and discission of the common carotid artery in seven cases of spontaneous subarachnoid hemorrhage due presumably to leaking aneurysms. Wechsler and Gross[28] in 1948 advocated arteriography and ligation of the common carotid artery not only in subarachnoid hemorrhage due to leaking aneurysms but also in some cases of cerebral vascular malformations. Wechsler, Gross, and Cohen[29] in 1951 reported the results of common carotid ligation in the neck in 30 cases. There were 17 aneurysms of the circle of Willis with only one death.

Method

The location of the aneurysm must first be accurately established by cerebral angiography, and the competency of the communicating arteries in providing an adequate blood supply to the brain must also be ascertained. Unilateral carotid puncture with compression of the opposite carotid artery during injection of the radiopaque medium with an anteroposterior x-ray exposure will usually provide the desired information. If satisfactory visualization of both sides of the anterior portion of the circle is not obtained by this method, then bilateral carotid angiography becomes essential. The treatment of the ruptured intracranial aneurysm during pregnancy does not differ materially from the treatment of such lesions where pregnancy is not involved. The principles are the same, hemorrhage must be stopped, recurrence of bleeding must be prevented, and an adequate blood supply to the brain must be provided if neurological complications are to be avoided.

In most instances, bleeding from a ruptured intracranial aneurysm stops if the pressure within the aneurysmal sac is reduced. Ligation of the carotid artery in the neck reduces the systolic blood pressure above the point of ligation about 50 per cent, and the pulse pressure by about 75 per cent, thus clotting takes place in the aneurysm and further bleeding is prevented. Recurrent hemorrhage rarely occurs after carotid ligation. One most serious objection to carotid ligation is the occurrence of neurological complications in some cases. The incidence of such complications has varied greatly in the statistics of different operators. Common carotid artery ligation is done only if the patient tolerates occlusion for at least 15 minutes.

Case Report

The patient was a 28-year-old white primipara in the eighth month of pregnancy. She had always been in good health and her pregnancy up to the present illness had been uneventful. Two weeks before admission to the hospital, while at home shaking a rug, she felt a sudden pain in the top of her head and the back of her neck. During the next few days she improved, but five days later the head pain recurred and she was admitted to her local hospital. Spinal puncture showed a grossly bloody fluid. The patient improved for about ten days but then had a recurrence of severe head and neck pain. Spinal puncture at this time revealed old and fresh blood and the patient was admitted to the Mount

Sinai Hospital. She was confused and disoriented. The blood pressure was 136/74. Temperature, pulse rate, respirations, and urine were normal. There was marked nuchal rigidity. The fundi showed early papilledema. There was a slight right central facial paresis and a positive right Babinski sign. Thirty-six hours after admission the right pupil became slightly larger than the left. On releasing the right common carotid artery after a period of digital compression, the patient complained of a pounding pain in the head. Release after compression of the left common carotid artery did not cause head

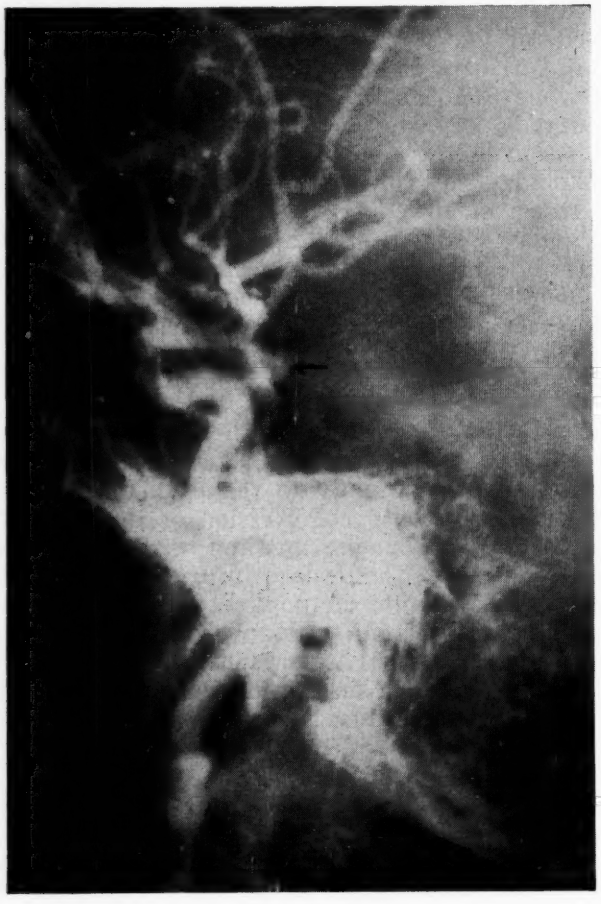

Fig. 1.—Aneurysm springing from bifurcation of right internal carotid and posterior communicating arteries.

pain. At this time both common carotid arteries were exposed under Pentothal anesthesia after an endotracheal tube had been passed. Local 1 per cent procaine was used as a supplementary anesthetic. Angiography was carried out with two injections each of 10 c.c. of 35 per cent Diodrast into the right common carotid artery. During the second injection of Diodrast an anteroposterior x-ray exposure was made while the left common carotid artery was occluded with a rubber tape. The lateral films disclosed a berry aneurysm springing from the junction of the internal carotid artery and the right posterior communicating artery (Fig. 1). The anteroposterior view showed an adequate passage of Diodrast from the right carotid system to the left. This indicated a competent anterior collateral circulation. The right common carotid artery was occluded with a rubber tape for fifteen minutes. The patient was permitted to awaken. No untoward signs or symptoms developed. The right common carotid artery was then doubly ligated with braided silk.

The patient recovered rapidly following these procedures. The plan had been to deliver her by cesarean section at or about term three weeks later. However, ten days following carotid artery ligation, the membranes ruptured.

Delivery was by cesarean section. The patient and the newborn infant were discharged three weeks later.

Review of the Literature

There have been only 5 reported cases of a ruptured aneurysm of the circle of Willis during pregnancy or the early puerperium proved by angiography or necropsy.

Strohscheim and Suzuki[6] in July, 1947, reported one case of ruptured intracranial aneurysm during pregnancy proved at necropsy.

This patient was a 35-year-old, gravida ii, para i, admitted to the hospital two weeks before term with persistent occipital and frontal headaches of thirty-one hours' duration. On the fourth hospital day, the patient went into labor and a low cervical section was performed under ethylene-oxygen-ether anesthesia. Four days later, after a normal postpartum course, she lapsed into coma and died.

Necropsy findings revealed a ruptured aneurysm on the posterior communicating artery measuring 4 mm. in size. Microscopically, there was fresh hemorrhage within the subarachnoid space.

Rhoads[22] in September, 1947, reported 2 cases of congenital aneurysm of the circle of Willis associated with pregnancy, one proved at postmortem, the other a tentative diagnosis made by signs and symptoms.

The first patient had had three episodes of frank cerebrovascular hemorrhage over a period of twelve years. Her symptoms on various admissions included dizziness, fainting, unconsciousness, left-sided numbness, nuchal rigidity, pin-point pupils, pain in the left eye, swelling of the globe of the left eye, and vomiting. On three separate admissions after the recurrence of neurological symptoms the spinal fluid was found to be grossly bloody and under increased tension. No angiograms were performed. The patient was next admitted three months pregnant for consideration of a therapeutic abortion. A consultation was held and it was decided not to perform a therapeutic abortion, but that the patient should be sterilized forty-eight hours after delivery. Two months later the patient died following a generalized convulsion after being admitted in a semicomatose condition. At postmortem, a berry aneurysm of the circle of Willis was found.

The second case reported by Rhoads was of a 27-year-old patient who, on the ninth postpartum day, had sudden convulsions beginning on the right and becoming generalized, a positive Brudzinski sign on the left, and xanthochromic spinal fluid. There were no signs or symptoms of toxemia. The only symptoms before the convulsions were severe headaches. The spinal fluid pressure was 320 mm. of water. The patient recovered on repeated lumbar punctures and bed rest. The tentative diagnosis was rupture of a congenital aneurysm of the circle of Willis.

Herzig[30] in 1948 reported the following case.

A 34-year-old gravida ii, para i, was admitted in coma two months from term. She had a convulsion one hour prior to admission at which time a spinal tap revealed bloody fiuid, and a diagnosis of subarachnoid hemorrhage was made. The patient died undelivered after being in coma for five days, with a few lucid intervals. Postmortem examination disclosed a ruptured berry aneurysm of the right anterior cerebral artery.

Brehm[7] in 1951 reported the first case of an aneursym of the circle of Willis in pregnancy, proved by angiography and treated by carotid ligation.

A 33-year-old primipara, in the last trimester of a normal pregnancy, developed a sudden excruciating headache and nuchal rigidity with grossly bloody cerebrospinal fluid. For the next 10 days she was treated with repeated spinal taps and bed rest. On the fifteenth hospital day she became unconscious. An angiogram was performed which

showed an aneurysm involving the region of the origin of the posterior communicating artery. The right common carotid artery was then ligated. The patient improved rapidly and thirty-nine days later had a normal infant, delivered by cesarean section.

The earlier literature which we had originally intended to include in our statistical analysis, on closer evaluation can only properly be reported as subarachnoid hemorrhage of undiagnosed origin associated with pregnancy, possibly due to the rupture of a congenital aneurysm (Mondy,[12] Wagner,[15] Apajalahti,[16] Pancot and Gelle,[17] Guttmacher[19]).

In 1928, Eastman,[14] writing on puerperal hemiplegias, commented that, since 1904 when Rudolph von Hosslin,[13] a German neurologist, published a monumental study of the various puerperal paralyses in which he reviewed, among other types, 146 cases of cerebral palsy, scant attention has been paid to puerperal hemiplegia in either the obstetrical or neurological literature. When mentioned in textbooks it is usually discussed briefly as one of the rare complications of eclampsia. At that time Eastman felt that the number of cases von Hosslin was able to collect, as well as the 7 cases of his own, rated careful consideration, particularly in the matters of etiology and prognosis. Eastman's survey of the literature showed the same divergence of opinion as to the incidence of puerperal hemiplegia as is found today. Villa observed only 2 examples in 27 years among 10,000 deliveries, while Immelman, in the Frauenklinik of Berlin, saw 8 cases within two years. In none of these four reports is an aneurysm of the circle of Willis contemplated.

Comment

Ruptured congenital aneurysms of the circle of Willis end fatally in from 35 per cent to 50 per cent of cases without the added hemodynamic and vascular changes that occur during pregnancy and labor. There are significant factors in pregnancy that must be presented in the sequence of events preceding death in many of these patients. In any pregnancy there is an increased volume strain on the vascular system. With each hemorrhage the damage done to the vessel makes it more vulnerable to subsequent bleeding. Slemons[18] demonstrated considerable increase in pulse pressure in normal pregnancy, especially marked during the latter part. The increased blood volume during pregnancy, added to the fluctuation in the blood pressure inherent in the stress and strain of labor, superimposed on an already potentially disastrous aneurysm under even nonpregnant conditions, seems to make elective cesarean section the most logical method of delivery. A regimen of anesthesia which meticulously avoids the production of a hypertensive state and minimizes the danger of postoperative vomiting is most important. On the other hand, delivery per vaginam with terminal caudal anesthesia is satisfactory in those known to have rapid labors. The anesthetic of choice in cesarean section appears then to be a field block in a well-sedated patient. Ergotrate, with its possible hypertensive side effect, is strongly contraindicated. With the advent of toxemia of pregnancy, the hazards are greatly increased and heroic treatment is mandatory.

We believe that the high mortality associated with this disease warrants tubal ligation in those with conclusive proof of a previous subarachnoid hemorrhage caused by a ruptured aneurysm. By the same token, when this accident occurs in early pregnancy, therapeutic termination, if desired, seems justified.

The possibility of a concomitant aneurysm as a cause of intracranial bleeding in patients with hypertension is an interesting conjecture. Since it is not feasible to perform angiography during eclampsia, the high mortality following complicating cerebrovascular accidents should certainly be followed at necropsy by close inspection of the internal carotid artery and the circle of Willis for evidence of a ruptured aneurysm. Where autopsy permission cannot be obtained, we suggest the possibility of shedding further light on this subject by injecting contrast media into the carotid vessels of the cadaver, i.e., morbid angiography.

Summary

1. The history and literature of ruptured intracranial aneurysm during pregnancy are briefly reviewed.

2. The etiology, symptomatology, and prognosis are presented.

3. A case of ruptured intracranial aneurysm of the circle of Willis during pregnancy, with recovery, is reported.

4. The diagnosis by angiography and treatment by carotid ligation are stressed.

5. The added gravity pregnancy imposes on such vascular lesions has been shown by case reports.

6. Cases of obscure obstetrical death may represent undiagnosed ruptured intracranial aneurysms.

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IDIOPATHIC EPILEPSY IN PREGNANCY

Summary of the Literature and Clinical Study of Twenty Patients

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SEVENTEENTH century medicine indicted uterine vapors as the cause of convulsions. Twentieth century medicine has not yet established the relationship between pregnancy and epilepsy. This subject has been strangely neglected in the medical literature, even though it has been estimated that there are as many epileptic persons as there are diabetic and tuberculous persons.[1] Long series of pregnant diabetic and tuberculous patients are frequently reported: pregnant epileptic patients, on the other hand, are still being reported individually, although the commonly quoted incidence of unclassified epilepsy complicating pregnancy is 0.14 per cent.[2, 3] The exact incidence of maternal mortality from pregnancy complicated by epilepsy has never been determined, but it has been said that the pregnant patient with status epilepticus rarely recovers.[4] A relatively recent national meeting devoted to epilepsy,[5] whose proceedings occupy over 600 pages, did not mention the pregnant epileptic patient, although it was noted that emotional stress may precipitate an attack.[6]

That epilepsy is poorly understood is readily attested by the voluminous medical literature which has accumulated since de Sauvage[7] in 1795 described it as a chronic disease, thus differentiating it from eclampsia. There also exists a large volume of lay literature designed to acquaint both the patient and the public with the sociological problems peculiar to the epileptic patient.

Investigators have drawn diverse conclusions from studies of the epileptic patient (Table I). Many individual case reports have been published, among them being cases which started during pregnancy,[13, 14] in which convulsions occurred only during pregnancies or in the immediate puerperium,[13] or in which the most severe convulsions were during the birth of each child.[15] It was even denied at one time[12] that epilepsy could begin during pregnancy.

TABLE I. EFFECT OF EPILEPSY ON PREGNANCY; CONCLUSIONS FROM THE LITERATURE

CONCLUSION	REFERENCE
1. In general epilepsy is unchanged	8, 10
2. Epilepsy most frequently improves	9
3. Epilepsy becomes worse	11
4. If epilepsy changes, it becomes worse	12

Clinical and Experimental Approach

Various techniques have been utilized in an attempt to establish the basic cause, transmission, precipitating factors or "trigger mechanism," contributing

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conditions, and methods of control or cure. The most fruitful of these studies have yielded only scant information when viewed in the light of the centuries-old knowledge of epilepsy's existence. Thus attempts have been made to gain understanding of the disease through classification, and that of Penfield[16] (Table II) appears to be one of the most workable classifications from a clinical viewpoint. Hypnosis has been used effectively to distinguish epileptic from convulsion-like seizures.[17] Although there is some doubt[18] that the essential feature of epilepsy is the convulsion, it is worth while to note that various methods[19, 20, 21, 22] have been used for its experimental production in an attempt to isolate a "trigger mechanism." The conclusion has been reached[23] that in subjects with an epileptic constitution, hypocalcemia acts as a precipitating factor of epileptic seizures. Attempts have been made to implicate the adrenal glands[24, 25] as a causative factor in the production of convulsions.

TABLE II. CLASSIFICATION OF EPILEPSY ACCORDING TO PENFIELD[16]

1. Cerebral seizures
Cause: Encephalomacias, hypoglycemia, etc.
2. Focal cerebral seizures
Pattern: Jacksonian, motor, visual, etc.
Localization: right precentral or left occipital, etc.
Cause: scar of birth injury, tumor, etc.
3. Idiopathic epilepsy

Some of the most revealing studies of idiopathic epilepsy have resulted from genetic studies, particularly of twins,[26, 27] and the fact that the tendency toward idiopathic grand-mal epilepsy is an inherited one is now beyond dispute.

All types of convulsive disorders have provided a fertile field for electroencephalographic study.[28, 29] In addition to being a valuable diagnostic tool, electroencephalography has shown that most patients while normally pregnant have decreased cortical activity as compared to that of the postpartum state.[30]

Evidence has recently been presented to show that epileptic and schizophrenic individuals have a specifically antigenic alpha streptococcus.[31, 32]

The inability thoroughly to evaluate any treatment has been stressed.[33]

A Clinical Study of 20 Patients in 28 Pregnancies

It was recognized several years ago that even with a moderate-sized obstetrical service the pregnant epileptic patient was not uncommon in The Ohio State University Hospital. Even so, it soon became evident that the true incidence of epilepsy in pregnancy would be difficult to determine because of limited patient cooperation. Known epileptic patients would give a negative history on admittance to the delivery floor or on the first visit to the prenatal clinic. Generally speaking, the private patients tended to be the worst offenders in regard to the apparently deliberately inaccurate history, but the implication that this is largely due to the social stigma attached to the disease is not borne out by the long follow-ups available on the service patients, whose record of failures to keep appointments is far greater than that of the average patient followed in our clinic. Indeed, their voluntary discontinuation of medication is very comparable to that of the notoriously uncooperative "young" diabetic.

Patients Included in the Study.—During the period 1950-1954 and covering 7,379 deliveries, there were found 20 patients with typical grand-mal attacks and without demonstrable organic pathology. In addition to these 20,

an additional 9 patients were seen with grand-mal seizures but with insufficient history and diagnostic work-up for satisfactory evaluation. Of the 20 patients, 1 was a private patient and 19 were clinical cases, and this on an obstetrical service with a ratio of clinical to private patients of 3 to 2. It is impossible to give a fair estimate of the incidence of idiopathic grand-mal seizures in pregnancy.

All patients were seen by and followed with a neurological consultant and all were under active treatment immediately upon diagnosis. Six of the 20 patients had their first medical work-up for seizures when they were seen in pregnancy. Treatment consisted of phenobarbital and Dilantin either to the point of convulsion control or Dilantin toxicity. Those patients who became toxic to dilantin (without convulsion control) received either Mesantoin or an experimental anticonvulsant drug with amphetamine.

Statistical Data.—The 20 patients were seen with a total of 28 pregnancies, and when last seen had a history of 55 deliveries and 2 abortions. Fifteen patients were seen with 1 pregnancy, 5 with 2 pregnancies, and 1 with 3 pregnancies.

Seven patients gave a family history of having one or more relatives with "convulsions."

There was no correlation between menarche and onset of convulsions. Sixteen patients had the first convulsion prior to the first pregnancy, one immediately following her first delivery, and 3 patients had onset of seizures during a second, third, and sixth pregnancy, respectively. Two patients associated increased seizures with beginning of the monthly flow.

The frequency of attacks with pregnancy is shown in Table III. Those patients who grew worse with pregnancy did so despite increasing drug therapy. One patient whose convulsions were well controlled during pregnancy, had a convulsion immediately following delivery and also immediately after a lobectomy performed for a cholesterol pneumonitis.

TABLE III. FREQUENCY OF ATTACKS WITH PREGNANCY

1. More frequent	11
a. But fewer attacks with subsequent pregnancy	1
2. Unchanged	5
3. Less frequent	4

Table IV shows the other complications of pregnancy and delivery in the 28 pregnancies.

TABLE IV. OTHER COMPLICATIONS OF PREGNANCY SEEN IN THE 28 PREGNANCIES

1. Pyelitis	2
2. Severe edema without blood pressure or urinary changes	1
3. Marked placental degeneration with stillborn 7-month twins	1
4. Low transverse arrest	1
5. Partial abruptio placentae	1

The body build of this group of patients was almost without exception scaphoid. The average weight gain with pregnancy was only 20 pounds in spite of the fact that most patients were seen late in pregnancy and therefore had relatively little diet control.

Of the 28 patients, 27 were delivered vaginally with a variety of premedication and anesthesia, the only constant factors being adequate sedation and oxygenation. One secundigravida was delivered by cesarean section at eight months' gestation after twelve hours of status epilepticus controlled only by constant intravenous sedation, and after Pitocin infusion and rupture of the membranes had failed to induce labor. The mother regained consciousness twenty-four hours post partum; both she and her infant survived.

A patient with a clinically parallel case with identical electroencephalographic findings and also with grand-mal seizures well controlled with phenobarbital and Dilantin, developed uncontrollable status epilepticus at seven and one-half months' gestation and was delivered in a moribund state by cesarean section after induction of labor failed. She regained consciousness some forty-eight hours after her last sedation, and also survived. Her baby, weighing 1,325 grams, died. This case is not included in the current series because the diagnosis was oxycephaly with internal hydrocephalus and therefore it cannot be classed as idiopathic epilepsy.

Of the 28 pregnancies, 25 terminated with live births; 1 set of twins was stillborn at seven months; and 1 pregnancy terminated in spontaneous abortion at three months. There was no correlation between the infant's sex and the course of the patient's epilepsy.

Comment

It became apparent early in this study that for an adequate rapid diagnosis of the grand-mal epilepsy seen on this service, hospitalization of the patient is necessary. This obviously is not always possible. While electroencephalogram and x-ray studies can be done on an outpatient basis, lack of patient cooperation makes adequate outpatient evaluation almost impossible. For example, the patient delivered of stillborn twins at seven months' gestation had two weeks of daily seizures during the fifth month of her pregnancy. These seizures were unknown to her obstetrician "because," the patient stated, "a person just doesn't like to talk about things like that." Fortunately her seizures remitted spontaneously, but she might just as easily have progressed to status epilepticus. One method of compelling the patient to seek follow-up care is to limit the quantity of her medication at any one visit—a course which may well defeat its purpose.

It is impossible definitely to separate those patients with spontaneous relapse during pregnancy from those whose relapse was due to discontinuation of drug therapy. For this reason it is difficult to determine the effect of idiopathic epilepsy on pregnancy or of pregnancy on idiopathic epilepsy.

Clinically, however, it is most important to be able to distinguish the epileptic patient from the eclamptic patient in pregnancy. The patient who without warning or prior history suddenly has a convulsion during labor, delivery, or the puerperium may present an extremely difficult problem in diagnosis, since some patients have the "dry" type of eclampsia, and the elevated blood pressure and proteinuria may be either part of the toxemia or direct sequelae of the convulsion itself. A continuation of the convulsion despite usually successful therapy should suggest status epilepticus.[34] Elevated serum uric acid levels do not necessarily indicate eclampsia, inasmuch as such levels may also be due to a convulsion per se.[35] Unless the patient is fairly quiet the electroencephalogram is of little value since it will contain so much "somatic artifact" that interpretation must be deferred. The immediate treatment of any convulsion, however, irrespective of its cause, is sedation, and the correct diagnosis may usually be obtained by correlating the patient's clinical course with her history.

The rare patient with pregnancy nearing term and in status epilepticus is extremely difficult to manage clinically. Except for the barbiturates, the commonly used analeptic drugs are given orally and unfortunately both status epilepticus patients seen here, aside from being completely incapable of taking

oral medication, developed gastric dilatation so that constant suction was necessary. Bowel incontinence makes rectal administration of medication difficult. Medication can be given by intermittently clamping off the gastric tube and/or hoping some drug will be absorbed rectally before it is expelled. Under these conditions it is not possible to estimate accurately the quantity of absorbed drug, and the patient who develops drug toxicity has much the same symptoms as does the one with status epilepticus. The convulsions of the two patients here reported were controlled only after delivery was accomplished.

No explanation is offered for the low weight gain seen in this group of patients.

It would have been interesting to have done electroencephalograms on the newborn infants, but such facilities were not available.

Summary

A group of 20 patients with idiopathic grand-mal epilepsy were seen with 28 pregnancies. This is believed to be the only series limited to idiopathic grand-mal epilepsy in pregnancy and under modern analeptic therapy reported in the English literature. Included is one patient with idiopathic status epilepticus and the report of a clinically parallel case in a patient with oxycephalic status epilepticus, both of whom survived. As far as can be determined, idiopathic grand-mal epilepsy is without effect on pregnancy except for the patient with status epilepticus; the effects of pregnancy on idiopathic epilepsy are unpredictable. In this series the majority of patients had more frequent attacks with pregnancy.

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EFFECT OF HYDERGINE (DIHYDROGENATED ERGOT) ON PRE-ECLAMPSIA AND UTERINE CONTRACTILITY*

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SHORTLY after the favorable reports on dihydroergotamine appeared in the obstetrical literature, Wilhelm[13] reported on the use of Hydergine. He concluded that the duration of labor was shortened, that cervical edema was lessened, and that a dilating action on the cervix followed Hydergine administration. Although he attributed this action to an improved circulation, he noted that the drug was oxytocic. Rupp[11] reported on 60 patients given Hydergine. After 47 patients with pre-eclampsia were treated with Hydergine, he acknowledged 44 cures with three patients improved. He further stated that oliguria and anuria were relieved and that eclampsia was prevented.

In the medical literature there are many reports on the cardiovascular effects of Hydergine in the human being. Joseph[8] stated that Hydergine was an effective agent in treating hypertension. Goetz[7] reported that dihydroergocornine was the only pure sympathicolytic derivative and that the other dihydroergot alkaloids showed direct constrictor effects on peripheral vessels. Roberts[10] wrote that Hydergine behaved best in patients with organic occlusive arterial disease. He believed that vasospastic disorders were not benefited. Seibert[12] concluded that Hydergine relieved tubal spasm in hysterosalpingography and could therefore be used to differentiate a mechanical block from a functional spasm of the tube. Bennett[3] cited experimental and clinical evidence that dihydroergocornine was safer than dihydroergotamine in the prevention of cyclopropane- and epinephrine-induced cardiac irregularity. Since this mixture of dihydroergot compounds was thought to possess greater potentialities for reducing hypertension without causing uterine spasm, a study with Hydergine was carried out on a group of pregnant patients.

Study

Twenty-eight patients were selected from the clinic population of the Colorado General Hospital to study the effect of Hydergine upon uterine contractility during pregnancy and labor and its effect upon pre-eclampsia. Both internal and external tocography was done and the tocographic records analyzed as described by Reynolds, Harris and Kaiser.[9] The external tokodynamometer was used in 19 cases, while in 8 internal tocography was employed.

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One patient was studied by both methods simultaneously. Nineteen patients had pre-eclampsia of a mild to severe degree and 3 had uterine inertia. Frequent determinations of maternal blood pressure, pulse rate, and fetal heart tones were made. Dilatation of the cervix was determined by repeated rectal examinations. Twenty-one patients were in prodromal or early labor and 7 were not in labor at the time of drug administration. In the total group of patients there were 13 primiparas. The patients' ages ranged from 16 to 41 years and their gestational period from 33 to 40 weeks. The majority of patients received Hydergine as a single intravenous dose of 0.3 mg. This amount consisted of 0.1 mg. dihydroergocornine, 0.1 mg. dihydroergokryptine, and 0.1 mg. dihydroergocrystine, and was contained in a 1 c.c. ampule. Five patients received an additional 0.3 mg. during the course of study. Four patients were given a continuous intravenous drip of Hydergine ranging from 0.1 mg. per one-half hour to 0.3 mg. per one-half hour. Two patients received a single intravenous dose of 0.6 mg. of Hydergine (Table I).

TABLE I. CLINICAL DATA ON PATIENTS GIVEN HYDERGINE

PARITY	COMPLICATION	FETAL WEIGHT (GM.)	METHOD OF STUDY	LABOR	DOSE I. V.	COMMENTS
0	Pre-eclampsia, inertia	3,210	TKD	6 cm.	Drip	Nausea
i	Diabetes	3,700	TKD	None	Drip	Drowsy
0	Pre-eclampsia	1,370	TKD	2 cm.	Drip	Drowsy
0	Pre-eclampsia	3,400	TKD	4 cm.	Drip	
0	Pre-eclampsia	2,470	TKD	3 cm.	0.3 I.V.	Vomiting
0	Pre-eclampsia	3,830	TKD	3 cm.	0.3 I.V.	
0	Pre-eclampsia	3,770	TKD	None	0.3 (2)	Postural hypotension
ii	Toxemia	2,960	TKD	2 cm.	0.3 I.V.	
0	Pre-eclampsia	2,900	TKD	5 cm.	0.3 I.V.	
i	None	2,970	TKD	7 cm.	0.3 I.V.	
0	Pre-eclampsia, inertia	3,400	TKD	5 cm.	0.3 I.V.	
0	Pre-eclampsia	3,260	TKD	2 cm.	0.3 I.V.	
0	Pre-eclampsia	2,630	TKD	None	0.3 (2)	Postural hypotension
i	Pre-eclampsia	3,160	TKD	2 cm.	0.3 I.V.	Postural hypotension
iii	Pre-eclampsia	2,230	TKD	2 cm.	0.3 I.V.	
i	None	1,940	TKD	None	0.3 I.V.	
0	Pre-eclampsia	1,300	TKD	2 cm.	0.3 (2)	Stillbirth
0	Pre-eclampsia, inertia	2,410	TKD	None	0.3 I.V.	
0	Pre-eclampsia	3,400	TKD	None	0.3 I.V.	
iv	None	3,330	Cath.	None	0.3 I.V.	Pain
iv	None	3,760	Cath.	3 cm.	0.6 I.V.	Pain
i	None	3,000	Cath.	4 cm.	0.3 I.V.	Pain
i	None	3,170	Cath.	3 cm.	0.3 I.V.	Pain
i	Pre-eclampsia	2,970	Cath.	3 cm.	0.3 I.V.	
iv	None	3,720	Cath.	None	0.3 I.V.	Pain
i	Pre-eclampsia	2,090	Cath.	2 cm.	0.3 I.V.	Pain, nausea and vomiting
ii	Pre-eclampsia	4,340	Cath.	3 cm.	0.6 I.V.	Nausea and vomiting
iii	None	3,100	Both	3 cm.	0.3 (2)	

SUMMARY

Number of patients	28
External tocographic studies	19
Internal tocographic studies	8
Combined methods	1
Primiparas	13
Multiparas	15
Prodromal labor	21
Not in labor	7
Pre-eclampsia	19
Uterine inertia	3

Results

There was a very significant increase in the frequency of contractions and uterine work following Hydergine administration with little or no change in the intensity of contractions. In the 8 patients studied by the intra-amniotic fluid pressure method, the frequency of the contractions increased almost proportionately to the amount of drug given (Fig. 1). In 16 patients with pre-eclampsia whose cardiovascular changes were followed at regular 5 and 10

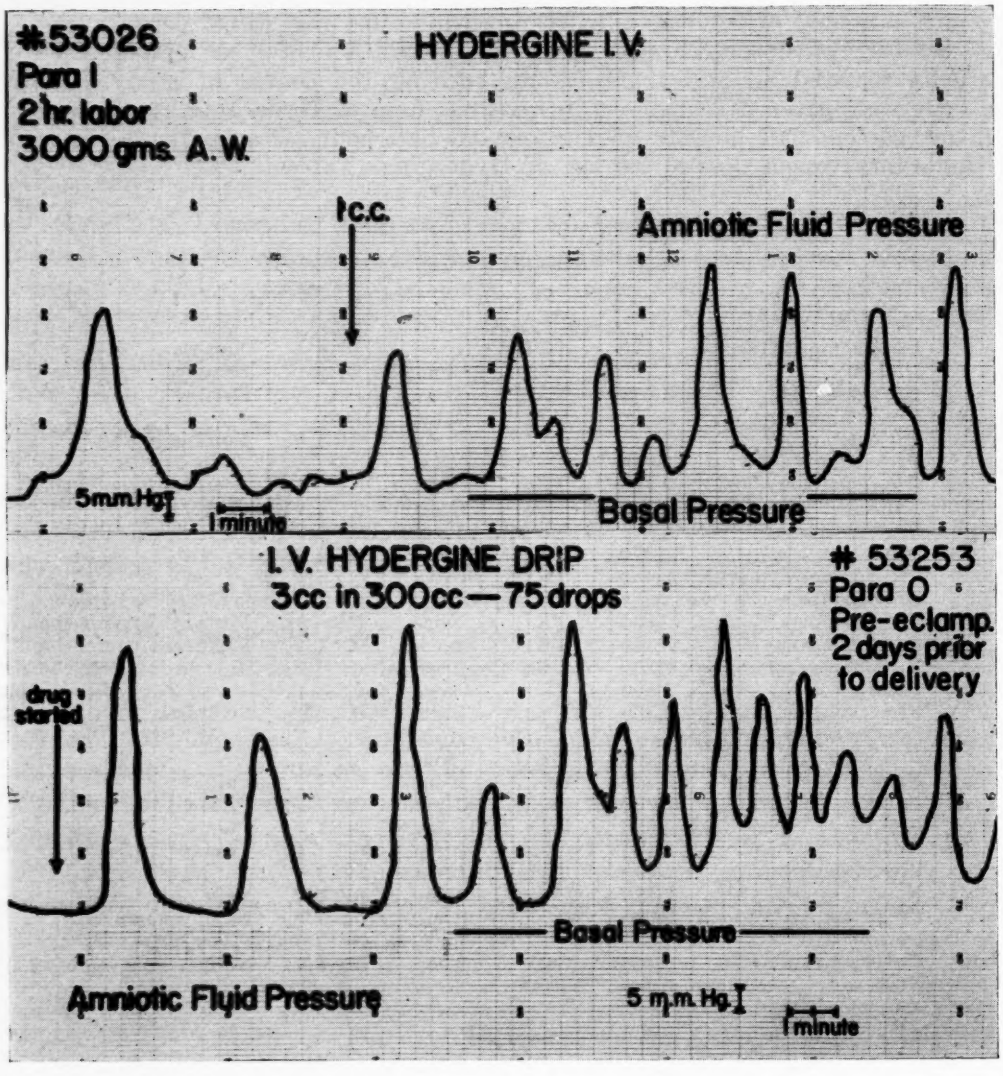

Fig. 1.—The effect of the dihydrogenated ergot preparation, Hydergine, on uterine contractility as measured by internal tocography, showing the increased frequency of contraction and elevation in basal tonus.

minute intervals, there was a fall of 5 mm. Hg in systolic blood pressure and 3 mm. Hg in the diastolic blood pressure. The maternal pulse rate in these patients increased slightly from 75 to 79 and the fetal heart rate decreased 5 points. In 9 normotensive patients the systolic pressure increased 7 mm. Hg and the diastolic 4 mm., while the maternal pulse rate declined from 75 to 73.

The fetal heart rate in the normotensive group decreased from 141 to 135 following Hydergine. No convulsions developed in any of the toxemic or normal patients given Hydergine. The side effects of the drug were drowsiness in 2 instances, nausea and vomiting in 5. In 6 patients an increase in pain was associated with uterine contractions following Hydergine. Postural hypotension occurred in 3 (Table II). The one fetal death which occurred during this study was due primarily to anoxia from prolapse of the umbilical cord.

TABLE II

A. FREQUENCY OF CONTRACTIONS FOLLOWING HYDERGINE

	n	nr	SD	SEM	CR	P
Control	27	1.31	±6.7	±13.1	4.5	.0001
Hydergine	27	2.5	±11.7	±25.0		

The difference between the observed means represents a highly significant increase in frequency of contractions following Hydergine administration. The role of chance as an explanation for the observed difference is less than 1 in 1,000. Correction has been made for sample size. The same highly significant differences exist between the controls and those given drugs when the uterine work was calculated.

B. MATERNAL PRESSURE, MATERNAL PULSE, AND FETAL HEART RATE

	MEAN BLOOD PRESSURE	MEAN PULSE	MEAN FETAL HEART RATE
16 Hypertensive Patients.—			
Control	144/97	75	139
Hydergine	139/94	79	134
9 Normotensive Patients.—			
Control	113/75	75	141
Hydergine	120/79	73	136

The difference between the observed means was not significant.

Comment

Gill[5, 6] has pointed out that the principal dangers surrounding the use of dihydrogenated ergot preparations in obstetrics are those of overdosage. He states that the important thing to know about any potentially dangerous drug is how to use it with safety. By careful clinical investigation he and his co-workers have shown that one of the dihydrogenated ergot preparations, in low dosage, can be used in the first stage of labor with some degree of safety. Others have emphasized that the dihydrogenated ergot preparations, because of their oxytocic properties, should be used only on indication and then with considerable caution.[4] Indeed, one report[2] states that dihydroergotamine should not be used because of the dangers of fetal loss and hematuria.

With the advent of hydrogenated ergotoxine alkaloids a newer pharmacologic agent, Hydergine, possessing greater muscle-relaxing properties and less toxicity became available. If, as claimed, this drug could relax the smooth musculature of blood vessels as well as the cervix without being oxytocic, this preparation would be ideal for treating the annoying complications of toxemia and prolonged labor. Favorable preliminary reports indicated that this premise was true. In this study, however, when the effects of Hydergine were subjected to the scrutiny of the more exacting methods of measuring uterine

forces, the oxytocic properties of this drug were easily and uniformly demonstrable. Hydergine, when given intravenously as a single dose or as a continuous drip, produced an increase in upper uterine segment activity. If dilatation of the cervix is roughly proportional to the work performed by the uterus, it may be assumed that any factor resulting in a significant increase in work would also produce a proportional increase in the rate of cervical dilatation. Since Hydergine qualifies as an oxytocic agent in the doses used, it follows that cervical dilatation would be expedited. The effects of Hydergine, however, if used intravenously, should not be compared to those in other studies where smaller intramuscular amounts are given, especially since ergot and dihydrogenated ergot are partially stored in muscle tissue.

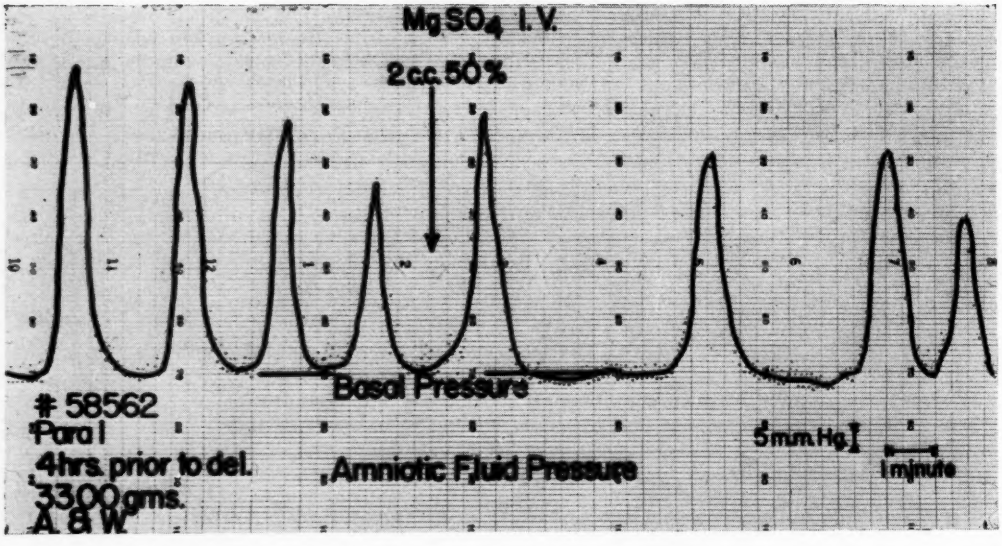

Fig. 2.—The effect of magnesium sulfate on uterine contractility as measured by internal tocography. It shows the marked relaxing effect of this drug and is recommended as an antidote for the "adverse" effects of any oxytocic agent.

No convincing evidence could be obtained from this study to show that Hydergine would "cure" toxemia of pregnancy or behave as an effective hypotensive agent in the treatment of pre-eclampsia. The magnitude of the cardiovascular changes and the small number of patients studied, however, prohibit the drawing of any definite conclusions relative to the precise effect of Hydergine on the vascular system of normal and abnormal parturients. Reflecting on the history of posterior pituitary extract it seems worth while to work out optimal dosages, methods, routes of administration, and indications for the use of the dihydrogenated ergot alkaloids rather than to condemn the preparations because of their residual oxytocic properties, only to have them used with abandon and without safeguards.

Abarbanel[1] demonstrated magnesium ions to have an immediate spasmolytic action on the tetanically contracted human gravid uterus, when injected intravenously. He reported that magnesium was effective when uterine tetany

had been induced by posterior pituitary extract, quinine, ergonovine, and Methergine. In this study, when 2 c.c. of 50 per cent magnesium sulfate was given intravenously, the frequency of contractions was greatly reduced and the basal tonus slightly decreased (Fig. 2). This drug should be used as an antidote whenever an adverse response occurs following the use of any type of oxytocic drug during the first stage of labor.

Conclusions

1. Twenty-eight parturients, 13 primiparas and 15 multiparas, were given Hydergine to study its effects upon uterine dynamics and pre-eclampsia.

2. Eight patients were studied by internal tocography, 19 by external recordings, and one by both methods simultaneously. The effect of Hydergine was observed in 16 patients with pre-eclampsia.

3. The amount of Hydergine usually used was 0.3 mg. given as a single intravenous injection. For study purposes, smaller and larger doses were given as an intravenous drip.

4. Amniotic fluid pressure, basal tonus, and frequency of contractions were increased in all patients given Hydergine and studied by the internal method.

5. Frequency of contractions and uterine work were increased following Hydergine in all patients studied by external tocography.

6. There were no significant changes in blood pressure, maternal pulse, or fetal heart rate following Hydergine in 16 hypertensive and 9 normotensive patients.

7. Twenty-five per cent of the patients who received Hydergine experienced mild to moderate side effects such as drowsiness, nausea, vomiting, pain, or postural hypotension.

8. Hydergine, in the doses used, still retained its ancestral oxytocic properties and did not ameliorate hypertensive disease of pregnancy.

9. Intravenous magnesium sulfate behaves as an effective spasmolytic agent in the treatment of induced uterine hyperactivity.

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A SIX-YEAR SURVEY OF MATERNAL MORTALITY IN THE CITY OF LOS ANGELES, CALIFORNIA (1945-1950)

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THE following data represent as much information as could be obtained about each maternal death that occurred in the City of Los Angeles, California, from 1945 to 1950, inclusive. This independent study accumulated information by analyzing each death certificate recorded in the Department of Vital Statistics of the City of Los Angeles. Whenever, it was possible, each physician in charge of the case was interrogated, or he was asked to return a questionnaire with pertinent information about each death. Whenever permission was given, hospital charts were studied. We have followed closely the method of study described by Newberger.[1]

The number of live births and fetal deaths that occurred in the City of Los Angeles from 1945 to 1950, inclusive, is shown in Table I.

TABLE I. LIVE BIRTHS AND FETAL DEATHS IN THE CITY OF LOS ANGELES (1945-1950)

YEAR	LIVE BIRTHS	FETAL DEATHS	TOTAL
1945	29,100	655	29,755
1946	34,388	728	35,166
1947	39,091	694	39,785
1948	37,911	685	38,596
1949	38,419	628	39,047
1950	37,905	644	38,549
Total	216,814	4,034	220,898

The number of live births, maternal deaths, and the number of maternal deaths per 1,000 live births are shown in Table II.

TABLE II. MATERNAL MORTALITY IN THE CITY OF LOS ANGELES

YEAR	LIVE BIRTHS	MATERNAL DEATHS	MATERNAL MORTALITY PER 1,000 LIVE BIRTHS
1945	29,100	52	1.78
1946	34,388	50	1.45
1947	39,091	47	1.20
1948	37,911	51	1.34
1949	38,419	34	0.88
1950	37,905	34	0.90
Total	216,814	268	1.23

The causes of the maternal deaths are shown in Table III. The ages of the mothers ranged from 15 to 45 years of age. Fifty-four and five tenths per cent of the maternal deaths occurred in the 15 to 30 year group, while 45.5 per cent of the deaths occurred in the 30 to 45 year group. In the first trimester, 76 (25.5 per cent) of the total number of deaths occurred. In the first trimester ectopic pregnancy and either hemorrhage or infection, principally from induced abortions, accounted for most of the deaths. Eight deaths (2.9 per cent) occurred

during the second trimester. In the third trimester there were 192 deaths, or 71.6 per cent of the total. Toxemia and hemorrhage were responsible for 150, or 78.1 per cent of the third-trimester deaths.

Of the maternal deaths, 35.5 per cent were due to hemorrhage, 20.5 per cent to toxemia, 20.5 per cent to infection, 6.4 per cent to cardiovascular conditions, 3.7 per cent to anesthesia, 8.2 per cent to embolism, and 5.2 per cent to other causes. Of the 95 patients whose deaths were attributed to hemorrhage, only 43 (45 per cent) were given whole blood as part of the treatment.

In the smaller hospitals there occurred 68 deaths, or 25.3 per cent of the total number. An indication of the kind of care given to the patients is suggested by the refusal of these institutions to participate in any way in this survey. In 1946, 10 per cent of the maternal deaths occurred in one small hospital.

TABLE III. CAUSES OF MATERNAL DEATHS

	1945	*1946*	*1947*	*1948*	*1949*	*1950*	*Total*	*% of Total*
Hemorrhage	25	21	9	16	11	13	95	35.5
Antepartum	3	3	1	2	2	2	13	
Postpartum	14	11	4	8	6	7	50	
Abortion	2	–	2	1	2	1	8	
Ectopic pregnancy								
Tubal	6	6	2	3	1	3	21	
Abdominal	–	1	–	2	–	–	3	
Toxemia	10	7	11	7	10	10	55	20.5
Pre-eclampsia	3	3	3	3	2	3	17	
Eclampsia	7	4	7	2	8	7	35	
Hyperemesis gravidarum	–	–	1	–	–	–	1	
Toxic hepatitis	–	–	–	2	–	–	2	
Infection	7	9	12	12	9	6	55	20.5
Puerperal	1	5	4	1	1	2	14	
Abortion	6	4	8	11	8	4	41	
Cardiovascular	1	2	5	5	2	2	17	6.4
Heart failure	1	2	3	5	5	2	15	
Hypertension	–	–	2	–	–	–	2	
Anesthesia	4	2	2	2	–	–	10	3.7
Spinal	2	1	1	2	–	–	6	
Inhalation	1	1	–	–	–	–	2	
Caudal	1	–	1	–	–	–	2	
Embolism	2	7	4	5	1	3	22	8.2
Other							14	5.2
Incompatible blood	1	–	–	–	–	–	1	
Intestinal obstruction	2	–	–	–	–	–	2	
(a) With bilateral salpingitis and an unruptured ectopic pregnancy	1							
(b) Following a cesarean section	1							
"Acute fright"	–	1	–	–	–	–	1	
Anemia	–	–	–	2	–	–	2	
Syncytioma	–	1	–	–	–	–	1	
Encephalitis with encephalomalacia	–	–	1	–	–	–	1	
Pulmonary hemorrhage (tuberculosis)	–	–	1	1	–	–	2	
Anaphylactoid shock	–	–	–	–	1	–	1	
Meningoencephalitis	–	–	1	–	–	–	1	
Dissecting aneurysm of left renal artery	–	–	–	1	–	–	1	
Bronchopneumonia with uremia	–	–	1	–	–	–	1	
Total	52	50	47	51	34	34	268	100.0

The type of operative delivery associated with the maternal deaths is shown in Table IV. Of the 65 deaths associated with some form of operative delivery,

41 (62 per cent) occurred where some type of cesarean section was performed. Ten deaths (15.3 per cent) were associated with version and extraction and breech extraction. There were 12 deaths (18.0 per cent) with forceps delivery.

TABLE IV. TYPES OF OPERATIVE INTERVENTION ASSOCIATED WITH MATERNAL DEATHS

	1945	*1946*	*1947*	*1948*	*1949*	*1950*	*Total*
Cesarean section	8	11	6	8	3	5	41
Low cervical	6	8	3	6	–	–	
Classical	2	–	3	2	3	4	
Porro section	–	3	–	–	–	–	
Extraperitoneal	–	–	–	–	–	1	
Version and extraction	1	2	1	–	–	1	5
Breech extraction	1	–	2	1	–	1	5
Forceps	2	7	–	–	1	2	12
Low	–	6	–	–	–	1	
Mid	1	1	–	–	1	1	
High	1	–	–	–	–	–	
Dührssen's incisions	1	–	–	–	–	–	1
Intravenous Pitocin	–	–	–	–	–	1	1
Total	13	20	9	9	4	10	65

Information regarding the infants was inadequate. There were 26 stillbirths (47 per cent) with the 55 deaths from toxemia. Seven stillbirths (7.3 per cent) were associated with the 95 maternal deaths due to hemorrhage. There were 3 stillbirths associated with the 17 deaths from cardiovascular disease and 3 associated with the deaths from anesthesia. There were 2 stillbirths with 22 maternal deaths from embolism.

Table V shows that autopsies were performed on 122 (45.4 per cent) of the mothers who died.

TABLE V. AUTOPSIES PERFORMED ON MOTHERS WHO DIED

YEAR	NUMBER PERFORMED	% OF THE TOTAL
1945	20	38.4
1946	15	30.0
1947	30	62.5
1948	27	55.0
1949	17	50.0
1950	13	37.1
1945-1950	122	45.4

It was difficult to obtain information about the quality of prenatal care given to the mothers who died. In 94 cases (35.0 per cent) the quality of prenatal care was considered to be adequate. In 53 cases (19.7 per cent) the prenatal care was definitely inadequate. Nothing concerning the prenatal care could be determined in respect to 121 (45 per cent) of the deaths.

Summary

An independent study was made of the maternal deaths associated with gestation in the City of Los Angeles from 1945 to 1950, inclusive. The study was effected through the compilation of information obtained by personal interviews with physicians and by studying hospital charts whenever it was possible to do so. There were 268 maternal deaths during this period.

Hemorrhage was responsible for 35.5 per cent, toxemia for 20.5 per cent, infection for 20.5 per cent, cardiovascular conditions for 6.4 per cent, anesthesia for 3.7 per cent, embolism for 8.2 per cent, and other causes for 5.2 per cent. Only 45 per cent of those patients who died of hemorrhage were given whole blood as part of the treatment. Twenty-five and three-tenths per cent of the total number of deaths occurred in the smaller hospitals. Cesarean section of one type or another was responsible for 62 per cent of the deaths that were associated with various forms of operative deliveries. The maternal mortality rate per 1,000 live births decreased from 1.78 to 0.90.

This independent study has emphasized that the proper dissemination of information on antepartum care should be stressed both to the laity and to the medical profession. The judicious use of whole blood in treatment of hemorrhage is obvious. The differential diagnosis between abortion and ectopic gestation should be stressed.

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FURTHER STUDIES ON THE RACIAL INCIDENCE AND MORTALITY OF ECTOPIC PREGNANCY

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IN A previous report[1] on the racial incidence of ectopic pregnancy, it was determined that there was one ectopic gestation to 177 total births in white women as compared to one ectopic pregnancy to 120 total births in Negro women. The most often quoted incidence of ectopic pregnancy is that of Schumann, namely, one ectopic to 303 intrauterine gestations. This ratio was obtained from data in Philadelphia hospitals during the year 1918. Using the same correction factors as Schumann, it seems probable that the actual incidence of ectopic gestation is greater than Schumann's statistics would indicate, and that the true ratio in white women is in the general neighborhood of one to 190 pregnancies and in Negro women one to 130 pregnancies. Our studies show that by both population and total birth analysis, there is approximately a 50 per cent higher incidence of ectopic gestation in Negro than in white women in the city of Baltimore, Maryland.

The role of chronic inflammatory disease was discussed in its relationship to the etiology of ectopic pregnancy. In view of the high incidence of gonorrheal infection in Negro women, the conclusion seemed inescapable that the differential in racial incidence of ectopic pregnancy reported in the previous paper was attributable to a higher incidence of pelvic inflammatory disease in Negroes. If this were true, the more efficacious methods of treating gonorrheal infection, now in widespread use, might well lead to a reduction of this frequent and grave complication of pregnancy. This general conclusion differs from that of Johnson and Post[2] who believe that the use of sulfonamides and antibiotics for acute salpingitis has been responsible in part for the increase in the number of ectopic pregnancies seen in the Charity Hospital in New Orleans. These authors feel that before these drugs were available many of the patients would have developed complete occlusion of the tubes. At the present time these infections in the tube are controlled before complete occlusion occurs. Fertility remains, but because of intratubal or peritoneal adhesions progress of the fertilized ovum is impeded and tubal implantation results. Krohn[3] also supports this concept on the basis of an increased incidence of ectopic pregnancy in his own private practice. In order to check our previous prediction of a reduction in the number of ectopic pregnancies and to confirm or refute the statements of Johnson and Post, it was decided to repeat the study of ectopic pregnancy in relationship to total births in the city of Baltimore.

The Present Study

As in the previous study, with the valuable aid of the record librarians, resident physicians, and chiefs of obstetrical and gynecological services of 18 hospitals within the population registration area of the city of Baltimore, the racial incidence of ectopic pregnancy in relation to total births during five years, 1949-1953, was determined. These data reported by individual hospitals are recorded in Table I. The wide variation in incidence recorded in Table I shows again how unreliable individual hospital statistics can be in showing the actual occurrence of ectopic pregnancy. The ratios of ectopic gestations to total births in white patients varied from 1:97 to 1:495. The variation in Negro patients is even more extreme with variations from 1:34 to 1:905. This can be explained by the fact that only 9 of the 18 hospitals in Baltimore admit Negro patients, as compared to 18 hospitals which admit white patients.

TABLE I. THE RATIO OF ECTOPIC PREGNANCY TO BIRTHS BY RACE IN 18 BALTIMORE HOSPITALS DURING A FIVE-YEAR PERIOD (1949-1953)

HOSPITAL	WHITE			NEGRO			COMBINED		
	EC-TOPIC	TOTAL BIRTHS	RATIO	EC-TOPIC	TOTAL BIRTHS	RATIO	EC-TOPIC	TOTAL BIRTHS	RATIO
Baltimore City	9	2,040	1:226	15	13,583	1:905	24	15,623	1:650
Bon Secours	28	7,199	1:257	0	0	-	28	7,199	1:257
Church Home	15	4,934	1:329	0	0	-	15	4,934	1:329
Doctors	1	3,266	1:3266	0	0	-	1	3,266	1:3266
Franklin Square	7	3,468	1:495	0	53	-	7	3,521	1:503
Johns Hopkins	46	6,661	1:144	200	6,957	1:34	246	13,618	1:55
Maryland General	25	6,221	1:248	0	0	-	25	6,221	1:248
Mercy	39	9,987	1:256	9	0	-	48	9,987	1:208
Provident	0	0	-	62	6,682	1:107	62	6,682	1:107
Saint Agnes	24	6,330	1:263	0	0	-	24	6,330	1:263
Saint Joseph	62	6,022	1:97	17	0	-	79	6,022	1:76
Sinai	55	12,903	1:234	7	430	1:61	62	13,333	1:215
South Baltimore	19	4,873	1:256	2	0	-	21	4,873	1:232
Union Memorial	26	7,914	1:304	0	0	-	26	7,914	1:304
University of Maryland	25	7,210	1:288	48	7,155	1:149	73	14,365	1:196
U. S. Marine	4	0	-	2	0	-	6	0	-
West Baltimore	67	10,564	1:157	0	1	-	67	10,565	1:157
Woman's	60	10,689	1:178	0	0	-	60	10,689	1:178
Total	512	110,281	1:215	362	34,861	1:96	874	145,142	1:166

The ratio of ectopic pregnancy to total deliveries by race in the 18 Baltimore hospitals during the five-year period, 1949-1953, was 1 to 215 in the white group and 1 to 96 in the Negro group, with a combined incidence of 1 to 166. In Table II we have made a comparison of the study on ratio of ectopic pregnancy to birth in Baltimore hospitals by race during the two periods, 1944-1948 and 1949-1953. There has been a slight decrease in the incidence of ectopic pregnancy in the second five-year period. This can be partially explained by the increased number of hospital deliveries during the two five-year periods. Since these ratios represented only hospital statistics, an attempt was made as in the previous study to correlate ectopic pregnancies with the total births during the same period in the population registration area for the entire city of Baltimore.* In Table III, the ratio of ectopic pregnancies to total births in Baltimore city, during the years 1949 to 1953, inclusive, is shown to be 1 to 178 for the combined white and Negro races. There was one ectopic gestation to 223 total births in white patients as compared to

*These data were kindly supplied by Mr. Todd M. Frazier, Director of Biostatistics of the Baltimore City Health Department.

TABLE II. COMPARISON STUDY ON RATIO OF ECTOPIC PREGNANCY TO BIRTHS BY RACE IN BALTIMORE HOSPITALS DURING THE PERIODS 1944-1948 AND 1949-1953

HOSPITAL	1944-1948						1949-1953					
	ECTOPIC		TOTAL BIRTHS		RATIO		ECTOPIC		TOTAL BIRTHS		RATIO	
	WHITE	NEGRO	WHITE	NEGRO	WHITE	NEGRO	WHITE	NEGRO	WHITE	NEGRO	WHITE	NEGRO
Baltimore City	13	7	1,745	6,034	1:134	1:862	9	15	2,040	13,583	1:226	1:905
Bon Secours	44	0	5,202	0	1:118	-	28	0	7,199	0	1:257	-
Church Home	25	0	5,081	0	1:203	-	15	0	4 934	0	1:329	-
Doctors	0	0	637	0	-	-	1	0	3,266	0	1:326	-
Franklin Square	37	3	6,849	0	1:185	-	7	0	3,468	53	1:495	-
Johns Hopkins	58	152	6,428	4,692	1:111	1:31	46	200	6,661	6,957	1:144	1:34
Maryland General	27	0	4,559	0	1:169	-	25	0	6,221	0	1:248	-
Mercy	31	5	7,641	0	1:246	-	39	9	9,987	0	1:256	-
Provident	0	33	0	4,765	-	1:144	0	62	0	6,682	-	1:107
Saint Agnes	63	0	7,043	0	1:112	-	24	0	6,330	0	1:263	-
Saint Joseph	53	10	6,432	0	1:121	-	62	17	6,022	0	1:97	-
Sinai	85	0	10,324	0	1:121	-	55	7	12,903	430	1:234	1:61
South Baltimore	29	2	4,663	0	1:161	-	19	2	4,873	0	1:256	-
Union Memorial	23	0	5,476	0	1:238	-	26	0	7,914	0	1:304	-
University of Maryland	34	45	6,676	4,367	1:196	1:97	25	48	7,210	7,155	1:288	1:149
U. S. Marine	2	1	1	0	-	-	4	2	0	0	-	-
Volunteers of America	0	0	1,377	0	-	-	-	-	-	-	-	-
West Baltimore	53	0	8.106	0	1:153	-	67	0	10 564	1	1:157	-
Woman's	27	0	7,273	0	1:269	-	60	0	10,689	0	1:178	-
Total	604	258	95,513	19,858	1:158	1:77	512	362	110,281	34,861	1:215	1:96

one ectopic pregnancy to 115 total births in Negro women. This indicates that ectopic pregnancy is more frequent in Negro than in white women, at least in the city of Baltimore.

TABLE III. YEARLY RATIO BY RACE OF ECTOPIC PREGNANCY TO TOTAL BIRTHS IN BALTIMORE CITY DURING THE YEARS 1949-1953

YEAR	WHITE			NEGRO			COMBINED		
	ECTOPIC	TOTAL BIRTHS	RATIO	ECTOPIC	TOTAL BIRTHS	RATIO	ECTOPIC	TOTAL BIRTHS	RATIO
1949	95	21,591	1:227	57	7,869	1:138	152	29,460	1:193
1950	97	21,104	1:217	85	7,909	1:93	182	29,013	1:159
1951	102	23,315	1:218	76	8,555	1:112	178	31,870	1:179
1952	106	24,132	1:227	85	8,623	1:101	191	32,755	1:171
1953	112	24,147	1:215	61	8,735	1:143	173	32,882	1:190
Total	512	114,289	1:223	364	41,691	1:115	876	155,980	1:178

A comparison of this study on the ratio of ectopic pregnancy to total births in Baltimore city in the white and Negro races during the years 1944-1948 and 1949-1953 is given in Table IV. Here it can be seen that although there were approximately the same number of ectopic pregnancies in the two periods, the number of total births increased 18,052 during the second five-year study. These data tend to contradict studies in the literature which infer that there has been an increased number of ectopic pregnancies in the last decade. The yearly ratios of ectopic pregnancies to total births in Baltimore city during a ten-year period, 1944-1953, are given in Table V.

TABLE IV. COMPARISON OF TWO STUDIES ON RATIO OF ECTOPIC PREGNANCY TO TOTAL BIRTHS BY RACE IN BALTIMORE CITY DURING THE YEARS 1944-1948 AND 1949-1953

RACE	1944-1948			1949-1953		
	ECTOPIC	TOTAL BIRTHS	RATIO	ECTOPIC	TOTAL BIRTHS	RATIO
White	604	106,818	1:177	512	114,289	1:223
Negro	258	31,110	1:120	364	41,691	1:115
Combined	862	137,928	1:160	876	155,980	1:178

TABLE V. YEARLY RATIOS OF ECTOPIC PREGNANCIES TO TOTAL BIRTHS IN BALTIMORE DURING A TEN-YEAR PERIOD, 1944-1953

YEAR	WHITE	NEGRO	COMBINED
1944	1:169	1:119	1:155
1945	1:185	1:104	1:158
1946	1:159	1:169	1:161
1947	1:187	1:130	1:170
1948	1:187	1:103	1:155
1949	1:227	1:138	1:193
1950	1:217	1:93	1:159
1951	1:228	1:112	1:179
1952	1:227	1:101	1:171
1953	1:215	1:143	1:190
Total	1:198	1:117	1:169

The data in Table V indicate that there has been a decreasing ratio of ectopic pregnancy to total births among white women which has been rather significant, whereas the incidence in Negroes has not been altered significantly. The combined racial incidence has also decreased significantly.

As in the previous report by using Schumann's correction factor the resultant data for the ten-year study in Baltimore would be as shown in Table VI.

TABLE VI. RACIAL INCIDENCE OF ECTOPIC PREGNANCY IN BALTIMORE FOR THE TEN-YEAR PERIOD, 1944-1953, USING SCHUMANN'S CORRECTION FACTOR

RACE	TOTAL ECTOPIC PREGNANCIES PLUS 10 PER CENT	TOTAL DELIVERIES PLUS 15 PER CENT	RATIO ECTOPIC TO TOTAL PREGNANCIES
White	1,228	254,273	1:207
Negro	684	83,721	1:122
Combined	1,912	337,994	1:177

Previously the true ratio of ectopic pregnancy in white women was reported to be in the general neighborhood of 1:190 pregnancies and in Negro women 1:130 pregnancies. This general statement could be modified, based on our ten-year study, to be 1:200 pregnancies in white women and in Negro women 1:120 pregnancies. It can thus be stated again that ectopic gestation is easily 50 per cent more common in Negro than in white women.

Mortality Studies on Ectopic Pregnancy

Since there is always great interest in the reduction of maternal deaths, it was desirable to determine the basic mortality in a large American city from ectopic pregnancy. In Table VII the mortality from ectopic pregnancy in the city of Baltimore, during the five-year period, 1949-1953, is listed. Here it can be seen that there was only one death in 512 white women with ectopic pregnancy during the five-year period, as compared to 9 deaths in 364 Negro women with ectopic pregnancy, giving a combined mortality for the five-year period of 1.14 per cent. Of the 10 deaths, 8 occurred in hospitals and 2 at home. These 10 deaths are difficult to analyze in respect to preventability. Only one of the 10 patients was operated upon. Eight of the 10 deaths were voted preventable by the Baltimore Maternal Mortality Committee. Three of the patients were not operated upon even though they were in the hospital as long as four to eleven hours after the diagnosis of ectopic pregnancy was made. Only one of the patients received 1,000 c.c. of blood during a four and one-half hour stay in a hospital. Despite the rather excellent reported mortality rate for a large city, it is possible that quicker diagnoses, more blood, and immediate surgery could have eliminated a certain percentage of these maternal deaths.

TABLE VII. MORTALITY FROM ECTOPIC PREGNANCY IN THE CITY OF BALTIMORE DURING A FIVE-YEAR PERIOD (1949-1953)

YEAR	WHITE			NEGRO			COMBINED		
	ECTOPIC	DEATHS	% MORTALITY	ECTOPIC	DEATHS	% MORTALITY	ECTOPIC	DEATHS	MORTALITY %
1949	95	0	-	57	1	1.7	152	1	0.65
1950	97	0	-	85	3	3.5	182	3	1.6
1951	102	0	-	76	1	1.3	178	1	0.57
1952	106	1	0.9	85	2	2.3	191	3	1.6
1953	112	0	-	61	2	3.3	173	2	1.15
Total	512	1	0.19	364	9	2.5	876	10	1.14

A comparison of the mortality rates from ectopic pregnancy in the two five-year studies in Baltimore is given in Table VIII.

TABLE VIII. COMPARISON OF MORTALITY RATES FROM ECTOPIC PREGNANCY IN BALTIMORE IN TWO FIVE-YEAR PERIODS

	PERIOD 1944-1948			PERIOD 1949-1953		
	ECTOPIC	DEATHS	MORTALITY %	ECTOPIC	DEATHS	MORTALITY %
White	604	4	0.7	512	1	0.19
Negro	258	10	3.9	364	9	2.5
Combined	862	14	1.6	876	10	1.14

From the data in Table VIII it can be pointed out that in a city of one million people it is possible to prevent death from ectopic pregnancy in white women. Incidentally, the single white woman who died was a nonresident but we have not deleted any death from this study on the basis of residency.

Since so many reports in the literature on mortality from ectopic pregnancy are based on hospital statistics it was of some interest to portray the individual hospital statistics over the last ten years in the city of Baltimore (1944-1953) (Table IX).

TABLE IX. DEATHS FROM ECTOPIC PREGNANCY IN 18 BALTIMORE HOSPITALS AND AT HOME IN THE TEN-YEAR PERIOD, 1944-1953

HOSPITAL	ECTOPIC PREGNANCIES	DEATHS	MORTALITY %
Baltimore City	44	2	4.5
Bon Secours	72	0	0
Church Home	40	0	0
Doctors	1	0	0
Franklin Square	47	0	0
Johns Hopkins	456	2	0.44
Maryland General	52	3	5.8
Mercy	84	0	0
Provident	95	5	5.3
Saint Agnes	87	0	0
Saint Joseph	142	3	2.1
Sinai	147	0	0
South Baltimore	52	0	0
Union Memorial	49	0	0
University of Maryland	152	5	3.3
U. S. Marine	9	0	0
West Baltimore	120	0	0
Woman's	87	0	0
Died at Home	4*	4	-
Total	1,740	24	1.38

*Two cases have been added as a correction of the previous report (1944-1948).

The individual mortality for the 18 Baltimore hospitals varied from 0 to 5.8 per cent. At least 12 of the hospitals have had no deaths for the entire ten-year period. It should be pointed out that these hospitals are limited to white women and the hospitals with the high mortality rates are caring for the Negro patients in Baltimore.

A general summary of deaths from ectopic gestation in the City of Baltimore during the ten-year period 1944-1953, is shown in Table X.

TABLE X. SUMMARY OF DEATHS FROM ECTOPIC PREGNANCY IN BALTIMORE IN THE TEN-YEAR PERIOD, 1944-1953

	ECTOPIC PREGNANCIES	DEATHS	MORTALITY %
White	1,117	5	0.45
Negro	623	19	3.04
Combined	1,740	24	1.38

The data in Table X tend to support the previously recognized fact that Negro women with ectopic pregnancy have a higher mortality rate, 3.04 per cent as compared to that of white women, 0.45 per cent. It will be seen, however, that some reduction of mortality in the Negro group is taking place in Baltimore if one compares the 3.9 per cent mortality rate of the five-year study, 1944-1948, with the 2.5 per cent of the five years, 1949-1953.

If the data on racial incidence obtained in this study were applied to the United States Vital Statistics for 1950 the hypothetical results shown in Table XI would be obtained.

TABLE XI. DATA ON RACIAL INCIDENCE AND MORTALITY OF ECTOPIC PREGNANCY OBTAINED IN THIS STUDY APPLIED TO UNITED STATES VITAL STATISTICS FOR 1950

	ACTUAL TOTAL BIRTHS REPORTED	ESTIMATED RATIO	ESTIMATED ECTOPIC PREGNANCIES	ACTUAL DEATHS REPORTED	ESTIMATED MORTALITY %
White	3,115,946	1:223	13,973	99	0.71
Negro	506,465	1:115	4,404	93	2.10
Combined	3,622,411		18,377	192	1.04

Although this is a statistical manipulation, it would set the general mortality rates from ectopic gestation in the United States in the year 1950 at less than 1 per cent for white women and 2 per cent for Negro women.

Comment

This study re-emphasizes that ectopic pregnancy is more frequent in the Negro women by about 50 to 60 per cent. In the previous study of the racial incidence it was predicted that a reduction in the number of these ectopic gestations would take place. Although in Negro women in Baltimore in the second five-year study this prediction has not been realized, the ratio of ectopic pregnancies to total births in white women has had a significant decrease. The explanation for this difference is not apparent at this time. At least in Negro women there has been no increase in the number of ectopic pregnancies. It is most difficult to obtain dependable statistical data on whether gonorrheal salpingitis is more common in Negro women, but many clinicians believe this to be an acceptable fact. In Baltimore, with a 20 per cent Negro population the reporting of gonorrhea in white and Negro women has been as given in Table XII.

TABLE XII. CASES OF GONORRHEA REPORTED IN BALTIMORE

YEAR	WHITE	NEGRO
1947	224	649
1949	96	740
1950	109	683
1951	121	691
1952	183	697
1953	186	812

There does not appear to be any great change in the number of reported cases of gonorrhea in the city of Baltimore. However these data may be interpreted, it appears that the prevention of gonorrhea is in some measure responsible for the variation in the incidence of ectopic gestation in white and Negro women.

Summary

The ratio of ectopic pregnancy to total births by race in the population area of Baltimore during the five-year period, 1949-1953, was one ectopic gestation to 223 births in white women and 1:115 in Negro women, with a combined incidence of 1:178. A previous five-year period, 1944-1948, showed an incidence of one ectopic gestation in 177 total births in white women and one ectopic pregnancy in 120 total births in Negro women, with a combined incidence of 1:160. Statistical analysis of these data comparing the two five-year

periods showed a significant decrease in the incidence of ectopic gestation to total births in white women, whereas the incidence in Negroes has remained unaltered. The combined racial incidence has also decreased significantly.

Applying the correction factors of Schumann to the ten-year study, 1949-1953, the general incidence of ectopic gestation would be in the neighborhood of 1 in 200 pregnancies in white women and in Negro women, 1 in 120. It can be stated that ectopic gestation is easily 50 per cent more common in pregnancies of Negro than of white women.

The mortality from ectopic pregnancy during the five-year period, 1949-1953, for the entire city of Baltimore was 0.19 per cent for white women and 2.5 per cent for Negroes, with a combined racial mortality of 1.14 per cent (876 cases with 10 deaths). For the ten-year period, 1944-1953, there were 1,740 women with ectopic pregnancy in Baltimore with 24 deaths, or a mortality of 1.38 per cent. Twelve of the 18 general hospitals in Baltimore have not had a death in the last ten years due to ectopic gestation.

In view of the high reported incidence of gonorrheal infection in Negro women, the conclusion seems inescapable that the differential in racial incidence of ectopic pregnancy is attributable to a higher incidence of pelvic inflammatory disease in Negroes. The use of antibiotics in the treatment of these diseases apparently has not increased the frequency of ectopic pregnancy in Baltimore.

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AFIBRINOGENEMIA: A PRESENTATION OF CASES*

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FAILURES in blood coagulation, although rare, have received increasing attention.[1-10] The physiology of blood coagulation is still not entirely clear; in fact, it is almost impossible to make a statement regarding it without challenge.

Fibrinogen, the material cause of the blood clot, is present in normal plasma in more than optimum amounts for coagulation.[11] Fibrinogenemia severe enough to result in massive hemorrhage is uncommon but apparently does occur.

Two possible explanations have been offered in the literature for depletion of the plasma fibrinogen. One involves the destruction of fibrin by fibrinolysin which is normally carried in the globulin portion of the blood. The other involves the immobilization of fibrin by thromboplastic substances released in the blood stream, with resultant intravascular clotting. These thromboplastic substances could enter the blood stream by amniotic fluid infusion or embolism.

Because cases of the type presented are rare we have included in our discussion a suggested method of treatment in detail.

Discussion

CASE 1.—M. R., a 25-year-old primipara, type A, Rh positive, was admitted to the French Hospital on Aug. 21, 1950, for control of moderate pre-eclampsia of less than one week's duration. Her antepartum course had been previously uncomplicated and her expected date of confinement was August 17. The patient complained of headaches and blurred vision and, on admission, the blood pressure was 150/90 with 4 plus edema and 4 plus albuminuria. The blood uric acid was 5.2 mg. per cent and urea nitrogen 12 mg. per cent. No improvement was noted on conservative therapy.

Induction of labor was twice attempted with castor oil and enemas, and on the fourth hospital day a Pitocin infusion was begun. Contractions then occurred every two to four minutes and were of good quality. After two hours the membranes ruptured spontaneously and the cervix was two fingers dilated. Thereafter contractions occurred every one and one-half to two minutes and after a labor of three and three-quarters hours the fetal heartbeat disappeared. The cervix was fully dilated at this time and within twenty minutes a stillborn male infant was delivered, weighing 7 pounds, 7 ounces, by midforceps under gas-oxygen-ether anesthesia.

During the next two minutes, while the placenta was delivered intact, bleeding was estimated at 1,000 c.c. The uterus and vagina were packed and transfusions started. The patient remained in good condition while the episiotomy was being repaired, but she bled through the packing and, despite receiving 1,500 c.c. of whole citrated blood, went into pro-

*Presented at a meeting of the New York Obstetrical Society, Jan. 12, 1954.

found shock within two hours after delivery. The packing was therefore removed, a small sulcus tear discovered and repaired, and the uterus repacked. Two thousand cubic centimeters of blood was given during the next hour without improvement in the patient's condition. "Cutdowns" were done on both ankles and 750 c.c. of plasma was given, while more blood was being obtained.

Thereafter, despite continuous transfusions, the patient remained in shock, with the blood pressure only occasionally obtainable. Five and one-half hours after delivery a supracervical hysterectomy was done under cyclopropane anesthesia. There was temporary improvement in the patient's condition, although it was noted at this time that the escaping blood showed no tendency to clot.

With continuous transfusions her condition remained fair until four hours after operation when she again went into profound shock, with evidence of additional bleeding from the episiotomy and venepuncture sites. The patient died sixteen and one-half hours after delivery, after receiving a total 9,000 c.c. of whole citrated blood and 750 c.c. of plasma.

The prothrombin time taken on two occasions showed no end point until thromboplastin was added and no specimen of blood showed clot formation.

Comment.—

In retrospect, the sequence of events in this patient's labor seems similar to that of a number of cases now recorded in the literature. There was a tumultuous type of labor, with evidence of premature separation of the placenta, massive hemorrhage, and evidence of failure in the blood-clotting mechanism. This is probably an example of amniotic fluid infusion.

CASE 2.—E. S., a 28-year-old primipara, type B, Rh negative, was admitted to the French Hospital on Oct. 10, 1951, for control of moderately severe toxemia. Her antepartum course had been previously uncomplicated, the expected date of confinement was November 7, and she had suffered from headaches, "eye strain," and swollen feet for one week.

On admission the blood pressure was 170/99, with 1 plus ankle edema and hyperactive reflexes. Fundascopic examination showed some spasm of the arterioles. The albumin was 3 plus, uric acid 6 mg. per cent, and urea nitrogen 6 mg. per cent.

There was no improvement on a strict toxemia regimen, so termination of pregnancy by cesarean section was decided on. In view of the previous case, Lee-White coagulation time, platelet count, and prothrombin time determinations were made just prior to the operation and were normal. On October 13, a low-flap cesarean section was performed under local and cyclopropane anesthesias, and an apparently normal 6 pound boy was delivered. There was remarkably little blood loss at operation.

The postoperative course was smooth until twenty-nine hours post partum, when the patient had a shaking chill and the temperature rose to 103° F. Thirty-four hours after operation the abdominal dressing was wet and inspection showed free bleeding through the skin incision, with normal lochia. The skin clips were tightened and then a pressure dressing was applied. Signs of internal hemorrhage became evident an hour later, when the blood pressure dropped to 90/70 and the patient became pale and restless.

Transfusions were begun and the patient was returned to the operating room where, under cyclopropane anesthesia, the abdomen was reopened through the same incision. There was free bleeding from every cut surface, and multiple oozing points beneath the flap and along the uterine suture line. In addition, there was about 1,500 c.c. of liquid blood in the peritoneal cavity which showed no tendency to clot. The abdomen was therefore quickly closed, using heavy silk through-and-through sutures in an attempt to aid hemostasis.

The patient had received 2,500 c.c. of blood during the procedure and left the operating room with a blood pressure of 120/76.

Over the next forty-eight hours the patient received 12 Gm. of fibrinogen in 2 Gm. doses at spaced intervals, 12,000 c.c. of blood running continuously, 10 mg. vitamin K every four hours, 25 mg. of cortisone twice, as well as continuous oxygen therapy and Wangensteen suction. The blood pressure was maintained well above shock levels throughout, but she was often slightly cyanotic and developed a heart murmur with marked tachycardia.

Clotting was noted for the first time in the laboratory fourteen hours after the onset of the bleeding, when a small clot was observed, and fibrinogen was detected in small amount. Clinically, clotting was not noted until thirty-six hours after the exploratory operation, although the bleeding continued vaginally, abdominally, and from injection sites for another eight hours, after which it ceased rather abruptly. Fibrinolysin was determined by the method of MacFarlane and Biggs[7] against fibrinogen in dilution. Dissolution of the clot after two hours' incubation at 37° C. was recorded.

For the first ten days postoperatively the course was febrile despite large doses of antibiotics and on the eighth day a superficial thrombophlebitis of the right calf was treated with lumbar sympathetic block and an Ace bandage. After the twelfth day, the patient was ambulatory, but the temperature rose again on the twenty-third day, when she had clinical and radiological evidence of a small pulmonary embolism. She was treated with Tromexan for five days, and discharged improved on the fifty-second hospital day.

Comment.—

Of particular interest in this case are the laboratory findings *before,* during, and after the occurrence of hemorrhage. The interval between the emptying of the uterus and the onset of hemorrhagic manifestations is difficult to explain on the basis of the mechanisms suggested by Reid, Weiner, Roby, and others. This case may be a combination of hypofibrinogenemia and excessive fibrinolytic activity.

CASE 3.—G. L., a 31-year-old multipara, gravida iii, para ii, type 0, Rh positive, was admitted to the French Hospital on May 13, 1953, for threatened abortion. Her last menstrual period was in December and her pregnancy was uncomplicated until an hour before admission when she began to have cramps and heavy vaginal bleeding. According to her past obstetrical history, she had had an uncomplicated twin delivery in 1947 and a spontaneous abortion at twenty weeks' gestation in 1952, following which she bled profusely, but not enough to be transfused.

On admission, the blood pressure was 140/90 and the fundus was at the level of the umbilicus and tender. No fetal heartbeat was heard and the patient was observed to bleed heavily with each uterine contraction. The blood pressure soon began to fall, and transfusions were begun, along with Pitocin infusion to hasten the emptying of the uterus.

Throughout labor, the patient was given 750 c.c. of blood, although she was losing approximately 25 c.c. with each contraction, and was oozing blood from the gums and from the site of a tooth extraction five days previously. One hour before delivery she vomited about 500 c.c. of liquid blood and it was noted at this time that the vaginal blood did not clot. Tests were then made on the original sample of blood taken for cross-matching and showed: normal platelet count, no end point on the prothrombin test, no fibrinogen, and demonstrable fibrinolysins.

Seven and one-half hours after the onset of cramps the patient expelled a 12½ ounce dead fetus in an intact sac with obvious abruptio placentae, and promptly lost 1,000 to 1,500 c.c. of liquid blood vaginally. One thousand cubic centimeters of whole citrated blood was rapidly pumped in while the uterus was compressed manually for forty-five minutes. This replacement was rapid enough to prevent shock and the patient remained alert and responsive throughout.

Difficulty in keeping the veins open was a major problem, and eventually a cutdown was done on one ankle but soon had to be abandoned. Only one arm vein remained open and there were large hematomas around all the others.

She had received 3,500 c.c. of blood by the time fibrinogen was obtained, five hours after delivery, and the laboratory reported for the first time a small clot formed that later dissolved. The first gram of fibrinogen was injected in 50 c.c. of sterile water, but the mixture was so viscous that it was impossible to inject the last 5 c.c. The patient immediately developed generalized giant urticaria, so the other 2 Gm. was dissolved in 1,000 c.c. of sterile water and given slowly over one and one-half hours. The first clinical evidence of clotting appeared two hours after the initial dose and blood drawn an hour later showed clot forma-

tion but no retraction, a gel end point prothrombin, and less than 100 mg. per cent fibrinogen. Fibrinolysin titer showed slight lysin after twenty-four hours of incubation. Subsequent samples drawn every two hours showed fibrinogen levels of 186 to 250 mg. per cent.

In the first eleven hours after delivery, the patient received 4,500 c.c. of blood and 3 Gm. of fibrinogen and showed marked improvement. An hour later, however, she again vomited blood and the vaginal bleeding increased again. She was given 3 Gm. of fibrinogen in 200 c.c. of sterile water, and a saphenous cutdown was done in the right thigh and a flexible polyethylene catheter threaded far into the vein.

After the second unit of fibrinogen the bleeding diminished somewhat again, but it was deemed advisable, in view of the transient nature of the previous improvement, to administer a third unit in the same manner. Complete cessation of bleeding occurred twenty-five hours after admission.

The patient had received a total of 5,750 c.c. of blood and 9 Gm. of fibrinogen. The rest of her hospital course was uneventful, except that one more transfusion was given for anemia. She was discharged in good condition on the seventh postabortal day.

Comment.—

We believe this to be the earliest gestation reported in connection with afibrinogenemia. The fact that the products of conception were expressed intact with no gross evidence of ruptured membranes is of interest.

Comment

When a diagnosis of hypofibrinogenemia has been made, we suggest the following measures:

First, of course, transfusion, preferably of whole blood, must be started. In the course of the first venepuncture, enough blood should be drawn to permit cross-matching against many pints of blood and to permit the use of 10 c.c. for the clot observation test, and to make available to the laboratory 20 c.c. for test purposes.

Venepunctures are of fleeting value and veins are precious in these cases. Infiltration at the site of venepuncture is the usual occurrence. We have encountered nothing as satisfactory as bilateral cutdowns on the saphenous veins with the insertion of flexible plastic tubing rather than the usual rigid cannula. Once effected, these cutdowns on the saphenous veins should give the obstetrician assurance of unimpeded entrance to the venous system for indefinite periods.

We believe that five pints of compatible blood should be available in reserve at all times. We have not used fresh blood in any of our cases, although some workers believe this is better, but this belief is without clear scientific evidence. Just as in preparation for a major operation, the use of one arm should be reserved for the blood pressure cuff and pulse determinations. The rate of transfusion may then be guided, in part, by the very frequent blood pressure readings.

To obtain fibrinogen, at the present time, may require many hours. In the face of massive hemorrhage, 9 Gm. of fibrinogen should be sought. The first 3 Gm. may be administered rapidly, dissolved in 200 c.c. of slightly warmed water. Thereafter, administration by the drip method with 3 Gm. dissolved in 500 or 1,000 c.c. of normal saline may be advantageous. Clinical observation, the clot observation test, and determination of blood levels of fibrinogen should be combined as indications of the amount of fibrinogen

needed. Blood samples drawn at least every hour will be required. In dealing with a fluctuating balance or imbalance between the various components essential in the clotting mechanism, the situation changes rapidly. The danger to these patients of death from hemorrhage or shock is apparent. It should not be permitted to overshadow the other serious hazards of renal shutdown or an overloaded circulation with cardiac failure. A catheterized urine specimen each hour is valuable. The cooperation of an experienced internist is invaluable. The services of the laboratory must, of course, be heavily relied on.

Summary

Three cases of afibrinogenemia are reported.

One case had a course similar to those reported by Reid, and co-workers as amniotic fluid infusion.

The second case, however, with its delayed bleeding and its high fibrinolysin titer, probably represents a combined coagulation defect.

The third case is possibly the first reported of afibrinogenemia in a gestation of only twenty weeks.

An outline of management is presented, with emphasis upon an adequate amount of fibrinogen, whole blood, routes of administration, and special attention to the treatment of shock.

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Discussion

DR. DUNCAN E. REID, Boston, Mass. (By special invitation).—The experience of a single individual with pregnant patients who some time in their clinical course exhibit an alteration in the clotting mechanism is limited. After hearing Dr. Heaton's paper, we can clearly see that these patients may differ in considerable detail from one another. It is obvious also that the initiating cause of the syndrome of incoagulable blood in pregnancy remains to be clearly defined.

Perhaps we might open the discussion by considering some of the features of blood clotting. Dr. Heaton has correctly implied that any scheme which depicts the events in the coagulation mechanism may soon become outdated due to the immense interest, work, and new knowledge being acquired in this aspect of hematology. In addition to the controversial aspects of blood clotting, the lack of universal terminology for the various elements which participate in the formation of the clot make it doubly difficult to interpret the various proposals which have been offered to explain the sequence of events in the coagulation mechanism. This criticism pertains particularly to the terms used to describe the factors which activate thromboplastin and those which either accelerate or deter the reactions concerned with blood coagulation.

Three basic reactions are involved in clot formation. The first of these is the preparation or activation of thromboplastin from a precursor present in the circulating blood. This is accomplished presumably by the interaction of the blood platelets with a plasma factor (i.e., thromboplasminogen or antihemophiliac globulin) which results in the liberation of thromboplastin. Then second reaction follows, namely, the conversion of prothrombin to thrombin. The final step is the formation of a fibrin clot through the interaction of thrombin and fibrinogen. In addition, normal clotting requires accelerator factors which are concerned primarily with prothrombin conversion or utilization. A labile component is contained in the plasma while the serum contains a more stabile component. Clotting may be delayed if these substances are not present in normal concentrations. Deficiencies in blood clotting may involve one or more of these substances, many of which are absent in the circulating blood at birth and the resultant diseases are regarded as genetic in origin. In addition, substances may appear which will decelerate the clotting process or dissolve the clot which has formed. These latter factors are not normally detectable in the circulating blood but appear under stress and shock and more especially with intravascular clotting.

In the cases under discussion the defect in the clotting mechanism is acquired, and believed to be caused by an inadequate concentration of fibrinogen. Previous clinical and laboratory observations attest to this concept. It has been postulated that the afibrinogenemia is the result of excessive intravascular coagulation brought about by the introduction into the maternal blood stream of thromboplastin derived from uterine contents. This is analogous to the sequence of events seen in defibrination experiments in dogs. The possibility exists that additional substances may be introduced into the maternal circulation from the uterine cavity which affect one or the other elements identified with the basic reactions of blood clotting.

It is generally felt that more than one of the factors involved in the coagulation process may be present in lesser amounts than normal whenever the clotting mechanism becomes upset. It would not be surprising to observe simultaneous deficiencies in some of the accelerator substances where the fibrinogen concentration is reduced to pathologic values. Indeed Ac-globulin has been reported to be depressed in such cases. It has been further suggested that there is a deficiency in the activation of thromboplastin from the plasma factor or antihemophiliac globulin. The most convincing evidence that this may occur is the clinical observation that the clotting difficulty may on occasion be corrected with relatively small amounts of Fraction I which contains antihemophiliac globulin as well as fibrinogen. However, it must be stated that the various elements which participate in blood clotting are present in considerable excess of the requirements for effective hemostasis. Hence, there must be a reduction in the concentration of these substances to 25 to 50 per cent of their normal values and in some instances to complete absence before the blood will fail to clot.

Tissues of the body react to injury by marshalling forces designed for either defense or repair. The blood is no exception and substances designed for such purposes are readily demonstrable in the circulating blood when intravascular clotting occurs. It has been shown recently in defibrination experiments in dogs that antithrombin was present during the time when the thromboplastic material was being infused, but disappeared from the circulation when the administration of the coagulant was stopped. The appearance of antithrombin presumably is an attempt on the part of the body to protect itself against further intravascular clotting.

Similarly, it has long been postulated that fibrinolysis-like activity occurs whenever there is intravascular clotting for the purpose of maintaining the patency of the blood vessel by dissolving the fibrin clot. Whether the fibrinolysin is present at all times but in undetectable amounts in the circulating blood, is a subject of some debate. The enzyme, however, is demonstrable in conditions of stress and in the presence of shock. Subsequent studies indicate that the endothelium of the capillaries is the probable source of this enzyme. The antagonist, antifibrinolysin, is believed to be under the control of the pituitary, adrenocortical, splenic systems.

The experience of our group leads us to believe that fibrinolytic activity in these patients is important with respect to ultimate hemostasis. In some instances the enzyme is barely

detectable while in others the amount may lead to clot dissolution even in the presence of adequate fibrinogen values (+ 100 mg. per cent). Dr. Heaton rightfully emphasizes the fact that fibrinolytic activity was a major factor in ineffective hemostasis in his second case. Why the onset of hemorrhagic diathesis was delayed is most difficult to explain. Apparently the case represents a variant in the coagulation difficulties of pregnancy. I am unaware of any similar case having been observed. Before drawing any final conclusions, however, I believe the patient should be restudied, keeping in mind the possibility of the diagnosis of thrombocytopenic purpura. It is well known that this disease tends to relapse in the early puerperium. The administration of cortisone may have masked her eventual symptoms of purpura by decreasing capillary fragility and increasing platelets.

A word of caution seems in order where intra- or postpartum hemorrhage is extensive. It is a dangerous philosophy to assume that the cause of the bleeding is an upset in the clotting mechanism. While the history and the type of case involved are significant, the diagnosis of a coagulation defect should be one of exclusion. Otherwise, hemorrhage from trauma or uterine atony will go undetected. One wonders if the initial difficulty in the first case was in part hemorrhage, the result of a traumatic sulcus laceration. Unquestionably, with excessive blood loss, a hemorrhagic diathesis can develop. Such a circumstance has been observed in surgical situations where blood loss to the point of exsanguination may be followed by an upset in the clotting mechanism. For purposes of this discussion this may have been the sequence of events in the first case.

Patients with an acquired hemorrhagic diathesis in pregnancy are easily recognized by the "clot observation test," where freshly drawn blood fails to clot in a test tube in the absence of an anticoagulant. While an afibrinogenemic state is believed the basic defect, other clotting factors, including antihemophiliac globulin, Ac-globulin, and to a lesser degree serum prothrombin conversion accelerator (SPCA), may become depressed. Whether these substances are ever reduced to the hemorrhagic range must still be demonstrated. Some of the more labile of these substances, however, may disappear from bank blood and this has a certain practical therapeutic implication. In these patients freshly drawn blood should be used whenever possible for transfusion purposes.

Adequate blood replacement supplemented with fibrinogen will not necessarily ensure a stable clot in the presence of marked fibrinolytic activity. The latter may continue to be a significant factor in the hemostatic mechanism until such time as the patient rallies from her shock. Whether a trypsin inhibitor would increase the antiproteolytic activity of the blood sufficiently to be of any therapeutic value is unanswered but its toxicity is well recognized.

Before closing we should like to make a few comments regarding the management of premature separation of the placenta as it pertains to the problem of afibrinogenemia. First, we have never observed a hemorrhagic diathesis except in the more severe forms of placental detachment. This means that of the total number of patients with premature separation, 90 per cent or less will not develop this complication. The time and method of delivery of the patients in this group are dictated largely by the maturity and condition of the baby in utero. In order to salvage the baby, cesarean section is frequently required.

The remaining 10 per cent of cases, or the severe group, may develop an afibrinogenemia. Immediate cesarean section continues to be the preferred method of treatment for the control of bleeding. We have questioned the advisability of this policy and have suggested a more conservative approach in the over-all management of the severe case. Those who oppose such a view believe that postponing cesarean section invites an incoagulable diathesis. Further, they believe that babies are lost unnecessarily. We have taken the position that the baby is already compromised. As a matter of fact, in the majority of these cases fetal death in utero has already occurred when the patient is first seen. Likewise, at the time the diagnosis of severe premature separation is made, the clotting mechanism is already disturbed. We do not question the method or necessarily the exact time of delivery. We strongly believe, however, that the status of the clotting mechanism must be positively known prior to surgery. If a firm, stable clot fails to form, the procedure should be postponed until the coagulation mechanism is restored to normal.

In résumé, Dr. Heaton feels that the first patient probably experienced an amniotic fluid embolism, the result of tumultuous labor. Pituitary extract may contribute to the latter, which re-emphasizes it as a drug with dangers when administered during the first and second stages of labor.

The second case is a most unusual one because while fibrinolytic activity played a major role in the upset of the clotting mechanism, the condition appeared late in the clinical course of the patient.

The third case presumably is associated with a fetal death in utero. The impression has existed among clinicians that patients with so-called "missed abortion" often bleed more than those who undergo spontaneous abortion prior to the tenth to the twelfth week of pregnancy. I suspect that the fetus was dead in utero for a longer period of time than was realized—perhaps three or fours weeks. I agree with Dr. Heaton that the patient developed an upset in the clotting mechanism primarily because of an afibrinogenemia through the medium of intravascular coagulation presumably initiated from thromboplastic material arising from within the uterus.

HEMORRHAGIC DIATHESIS WITH HYPOFIBRINOGENEMIA FOLLOWING FETAL DEATH IN UTERO

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IN RECENT years it has become evident that certain instances of hemorrhage during pregnancy or intra partum are caused by a disturbance of the mechanism of coagulation. The predominant number of such instances is accompanied by hypo- or afibrinogenemia,[1-6] while a minority of cases is due to a variety of other coagulation defects.[7, 8]

Hypo- or afibrinogenemia has been observed with the following three conditions: (1) abruptio placentae, (2) amniotic fluid embolism, and (3) fetal death during pregnancy. In the third condition systemic hemorrhagic symptoms (subcutaneous, intramuscular, gingival hemorrhages, etc.) usually precede blood loss from the uterus, while in the other two more acute syndromes, severe vaginal bleeding occurs without any premonitory signs elsewhere. The clotting defect in the acute hemorrhagic syndrome due to abruptio placentae is probably caused by intravascular coagulation with consequent depletion of fibrinogen, prothrombin, and Ac-globulin (= labile factor).[9] In amniotic fluid embolism it is not clear whether intravascular coagulation or fibrinolysis is the major etiological factor. Reid[6] claims that amniotic fluid embolism induces intravascular coagulation. The very low thromboplastic activity of amniotic fluid[17] and the delivery of intact ovisacs in a certain number of cases with hypofibrinogenemia speak against this theory. It appears more reasonable to assume that amniotic fluid embolism leads to shock and consequent fibrinolysis. One must also assume that the occasional demonstration of fibrinolysis in the presence of abruptio placentae is a secondary manifestation of shock due to blood loss after the mechanism of hemostasis has been disturbed by intravascular coagulation. Intravascular clot formation is believed to be set off by the entrance of retroplacental tissue extracts with high thromboplastic activity into the maternal circulation. The mechanism of autoextraction of retroplacental debris has been extensively studied in human beings and substantiated with animal experiments by Schneider[10] and by Page and associates.[11]

Because of the paucity of reports on hypofibrinogenemia secondary to fetal death during pregnancy, the abnormal coagulation mechanism in this condition has not been subject to extensive investigation. The most carefully studied case has been recently reported by Ratnoff.[5] His patient had hemorrhagic symptoms with marked hypofibrinogenemia and moderate hypoprothrombinemia for four and one-half weeks before hysterectomy. The author could not demonstrate

any increased fibrinolytic activity, and postulates that the clotting defect was due to intravascular coagulation secondary to the entrance of placental material with thromboplastic activity into the maternal blood stream.

The present report concerns a case of subacute hemorrhagic diathesis after intrauterine fetal death in which delivery was induced medically. The patient received only 250 c.c. of blood 2 days before delivery, and it was possible to study the changes in clotting factors during the course of the disease without the disturbing effect of large amounts of transfused blood or fibrinogen.

Methods

Fibrinogen Determination.—Precipitation of fibrin according to the method of Cullen and Van Slyke[12] and microKjeldahl nitrogen determination on the fibrin clot obtained from 1.0 c.c. of plasma with the method of Ma and Zuazaga.[13]

Prothrombin Time.—Method of Quick.

Prothrombin Concentration.—Modified two-stage method.[14]

Labile-Factor Determination.—Modified two-stage determination of prothrombin. Deficiency in labile factor results in a delay in prothrombin conversion which is correctable with fresh normal barium sulfate-treated plasma. The results were not converted into units using a standard reference table; the present report will state only whether there was an appreciable labile factor deficiency or not.

Bleeding Time.—Method of Ivy (normal up to 6 minutes).

Clotting Time.—Modified Lee-White method (normal up to 20 minutes).

Platelets.—Reese Ecker chamber count.

Fibrinolysis.—a. Observation of blood clots or of citrated plasma clotted with calcium chloride for 5 days at 37° C. for lysis.

b. Fibrin plate method of Astrup.[15]

c. Test tube method: 0.1 c.c. of 1 per cent fibrinogen solution and 0.1 c.c. of plasma or serum to be tested are placed in a Pyrex tube (75 by 8 mm.). This mixture is clotted with 0.1 c.c. of thrombin (10 National Institutes of Health Units per cubic centimeter). The tubes are incubated at 37° C. for 5 days and observed for lysis.

The fibrinogen solution is prepared by dissolving 100 mg. of dry bovine fibrinogen (Armour & Co.) in 9.5 c.c. of 0.9 per cent sodium chloride solution and 0.5 c.c. of imidazole buffer at pH 7.2.

Fibrinogenolysis.—Fibrinogen and plasma or serum are mixed as described in method "c" for fibrinolysis. After an incubation period of 20 hours at 37° C., 0.1 c.c. of thrombin solution is added to the mixture and observed for clottability. In the event of fibrinogenolysis, no clot is obtainable.

In order to avoid coagulation of fibrinogen by possible traces of thrombin present in the serum to be tested, all lysis tests were carried out with serum obtained from blood allowed to clot in plain glass for 6 hours at 37° C. By this time the sera were free of active thrombin.

Case Report

The patient was a 36-year-old white housewife, para ii, gravida iii, who was being followed during her third pregnancy as an outpatient at the University of Minnesota Hospitals. The first two pregnancies were uncomplicated. There was no personal or family history of hemorrhagic diathesis. The last menses started Aug. 4, 1952. The course of the pregnancy was perfectly normal until the end of the twenty-second week of gestation when the fetal movements disappeared and the fetal heart tones became inaudible. The patient was asymptomatic, and it was decided to wait until the product of conception would be delivered

TABLE I. STUDIES OF HEMOSTASIS BEFORE AND AFTER DELIVERY

TIME IN RELATION TO DELIVERY	FIBRINOGEN (MG. %)	PROTHROMBIN (UNITS/C.C.)	LABILE FACTOR	PLATELETS (PER C.MM.)	BLEEDING TIME	CLOTTING TIME	PROTHROMBIN TIME	
							PATIENT (SEC.)	CONTROL (SEC.)
4 days before	76			79,000	6 min., 30 sec.		15.1	11.0
2 days before	81	240	Decreased	84,000	6 min.	30 min.	18.2	11.9
Venisection of 500 c.c. of blood and transfusion of 250 c.c. of blood								
12 hours before	124	200	Decreased	116,000			16.0	11.9
Delivery								
12 hours after	112	180	Decreased	130,000			15.2	11.2
20 hours after	126							
40 hours after	149	285	Normal	168,000			12.2	11.6
3 days after	172			212,000				
5 days after	191				4 min., 30 sec.	17 min.		
14 days after	320	280	Normal	224,000			11.8	11.8

spontaneously. Exactly two months after fetal death, the patient developed large ecchymoses over the extremities and the abdominal wall. She returned to the hospital one week later and was admitted for induction of labor. The physical examination was negative except for the previously mentioned ecchymoses and a uterus consistent with a pregnancy of five months' duration. Vital signs were within normal limits including a blood pressure of 120/78. Before induction with intravenous Pitocin drip, a prophylactic transfusion of 500 c.c. of fresh blood was attempted, but had to be discontinued after 250 c.c. because of a severe chill. The reaction was not hemolytic in type. Plasma and urine did not show any free hemoglobin and a repeat cross-match with the application of the indirect Coombs test failed to detect any incompatibility. The first attempt at inducing delivery was unsuccessful. The second one, 48 hours later, resulted in the delivery of placenta and intact ovisac containing a macerated fetus which weighed 440 grams and was 30 cm. in length. The fetus was not hydropic. The estimated immediate postpartum blood loss was 220 c.c. The patient's course was uneventful from then on. She did not develop any new ecchymoses and was discharged on the fourth postpartum day.

Laboratory Studies on Admission.—Urinalysis was negative, hemoglobin 14.2 Gm. per cent, white blood count 7,950 per cubic millimeter with a normal differential count, sedimentation rate 4 mm. after one hour (Westergren), bleeding time 6 minutes, 30 seconds, clotting time 30 minutes, prothrombin time 15.1 seconds, control 11.0 seconds, platelets 79,000 per cubic millimeter, fibrinogen 76 mg. per cent, clot retraction good, serum bilirubin direct 0.1 mg. per cent, total 0.6 mg. per cent, cephalin cholesterol flocculation trace, thymol turbidity 3 units, zinc turbidity 6 units, total proteins 6.8 Gm. per cent, albumin 3.8 Gm. per cent, globulin 3.0 Gm. per cent, alpha globulin 1.3 Gm. per cent, beta globulin 0.5 Gm. per cent, gamma globulin 1.2 Gm. per cent (method of Milne[18]), serum cholinesterase 0.51 Δ (delta = absolute change) pH/hr., urine urobilinogen 0.5 mg. per day, urine coproporphyrin 394 gamma per day.

The changes in the patient's clotting mechanism before and after delivery are presented in Table I. Fibrinogen and platelets were the most affected factors. Their rise to normal after delivery was relatively slow. The drop in prothrombin and labile factor was not so pronounced and both factors returned to normal within forty hours after delivery. At no time was it possible to detect any fibrinogenolytic or fibrinolytic activity in the patient's plasma or serum, nor was there any evidence of increased thrombin inhibitory activity. The patient's blood collected two days ante partum was also assayed for its antihemophilic and stable factor activity by comparing the effect of the patient's blood with the effect of normal blood on the clotting defect of hemophilic (antihemophilic-globulin-deficient) and stable-factor-deficient blood.[14] The results obtained with normal and the patient's blood were identical. One can safely assume that the patient's antihemophilic globulin and stable-factor activity were not appreciably decreased at the time of hypofibrinogenemia. It should be mentioned, however, that minor changes in these two clotting facors cannot be detected with the applied comparative test methods. The prolongation of the clotting time and Quick's prothrombin time before delivery is the result of decreased concentrations of fibrinogen, prothrombin, and labile factor. In the presence of multiple coagulation defects, these two tests are unspecific. For detailed information, each clotting factor should be determined separately. The low sedimentation rate of 4 mm. in one hour is a well-known manifestation of low fibrinogen concentration. It is of interest that after recovery the sedimentation rate rose to 28 mm. concomitantly with a rise of fibrinogen to 320 mg. per cent. The coincidence of fibrinogenopenia, hypoprothrombinemia, thrombocytopenia and labile-factor deficiency in the presence of normal liver-function tests, without any evidence of fibrinogeno- or fibrinolysis, strongly suggests that the patient's hemorrhagic diathesis was caused by intravascular coagulation with consequent depletion of these clotting factors.

Comment

The pathogenesis of the hemorrhagic diathesis with hypo- or afibrinogenemia acquired during pregnancy or intra partum has not been absolutely established.

In acute abruptio placentae, Schneider's[10] theory of the release of thromboplastic substances from retroplacental debris into the maternal circulation best explains the clotting abnormalities thus far elicited in a certain number of carefully studied cases. If fibrinolysis were the only abnormality, one would not expect a concomitant drop of fibrinogen, prothrombin, and labile factor, which can be quite marked at times. A careful scrutiny of the cases where fibrinolysis has been demonstrated reveals that there was always an episode of shock. Hence it is most probable that the lysis of clots was a secondary manifestation.

The coagulation defect in hypofibrinogenemia secondary to fetal death during pregnancy also appears to be caused by intravascular coagulation. The data presented in this report and Ratnoff's[5] observations can be best explained by assuming that fetal death led to abruptio placentae and secondary release of highly active thromboplastic material into the maternal circulation. In practically all the reported cases, fetal death occurred between the fourth and sixth months of gestation. It usually took from one to four months until hemorrhagic symptoms developed.[1, 5, 6, 19, 20, 21] The frequent delivery of the placenta with intact ovisac, as in our case, strongly suggests that placental separation has taken place prior to the onset of labor. One may speculate that the onset of hemorrhagic manifestations coincides with the abruptio. The etiology of fetal death is multiple. Special emphasis has been placed on the fetal effect of maternal Rh sensitization. The majority of fetal deaths accompanied by hypofibrinogenemia have been ascribed to erythroblastosis.[1, 5, 6, 20] In our case the cause of fetal death could not be determined. No incompatibility could be detected between the parents' blood groups, and an indirect Coombs test performed on the father's erythrocytes after incubation with the mother's serum was negative (mother's type: A, CDe/cde, father's type: O, CDe/cde). There was no gross or microscopic evidence of erythroblastosis in the fetus or placenta.

The therapeutic management of this syndrome should be directed to achieving the following aims: (1) elimination of the source of intravascular defibrination; (2) replacement of depleted clotting factors.

Intravascular coagulation is set off by the entrance of retroplacental tissue extract into the maternal circulation. The removal of the placenta usually stops this mechanism. It should be mentioned, however, that in certain cases a complete hysterectomy had to be performed to achieve this purpose. The replacement of clotting factors can be done by transfusions of normal plasma, blood, or fibrinogen. The administration of fibrinogen is only a partial therapeutic measure, because recent studies, including our own, showed that prothrombin and the labile factor are decreased as well. It has the definite advantage, however, that fibrinogen can be replaced in high concentration in a relatively short space of time. The best therapeutic approach is probably an alternation of fibrinogen and plasma or blood transfusions. The untoward reaction to blood transfusion encountered in our case has not been reported before. It is obviously a very undesirable complication, but fortunately the patient did not require any further transfusion. The pathogenesis of this reaction was not elicited. There

was neither laboratory nor clinical evidence of hemolysis or allergic symptoms. It is of interest that the transfusion of 500 c.c. of the patient's blood collected two days ante partum caused the same type of reaction in a normal recipient. This suggests that the untoward effects might be related to the disease per se. One could, for instance, suggest a foreign-protein reaction secondary to intravascular coagulation. This transfusion was given to see if it would induce a depletion of clotting factors in the normal recipient. The result was only a temporary thrombocytopenia (fall from 192,000 to 124,000 per cubic millimeter) without any changes in concentration of prothrombin, fibrinogen, and labile factor. The minor drop in platelets cannot be interpreted as specific because it is known to occur after transfusions with or without reactions.[22] Fortunately, the incidence of such reactions in hypofibrinogenemic patients appears to be extremely rare and this major and essential therapeutic tool can be used with impunity.

Summary

1. A case of acquired hemorrhagic diathesis during pregnancy after fetal death has been described.

2. The clotting defect consisted in decreased concentrations of prothrombin, labile factor, fibrinogen, and platelets. There was no fibrinolysis. The temporary decrease of these clotting factors is believed to be due to intravascular clot formation after release of retroplacental tissue extracts with high thromboplastic activity into the maternal blood stream.

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A RAPID, SIMPLE SEMIQUANTITATIVE TEST FOR FIBRINOGEN EMPLOYING THROMBIN

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OBSERVATIONS made in recent years by several different groups of investigators[1-10] have established the finding of hypofibrinogenemia occurring in several complications of pregnancy; more particularly in patients who have severe premature separation of the placenta, longstanding intrauterine fetal death, or an amniotic fluid embolus.

Establishing definitely the diagnosis of hypofibrinogenemia requires some way of determining the plasma fibrinogen level. Since the quantitative determination of fibrinogen requires some time to accomplish, several *semiquantitative* methods have been proposed which can be used clinically to give at least some approximation of the blood fibrinogen levels. Of these methods the clot fragmentation test recommended by Weiner, Reid, and Roby[9] is perhaps the simplest test and requires no reagents besides the specimen of blood from the patient. Two other methods which have come to our attention require thrombin as a reagent in addition to the blood from the patient. One of these is the serial dilution method of Schneider[11] and the other the clotting test proposed by Allen.[12] All these tests have their relative advantages and disadvantages, some of which will be dependent on the subjective reactions of the individual practitioners.

We are describing another procedure employing thrombin as a reagent which seems nearly as simple as any of these procedures, which gives reasonably good results, and which can be completed a few minutes after the blood is drawn. It will give a definitive answer when the fibrinogen levels are normal at term, and when there is an actual absence of fibrinogen or afibrinogenemia. Intermediate levels of fibrinogen between these two extremes are more difficult to estimate.

This test depends in principle on the fact that thrombin added to plasma rapidly converts fibrinogen to fibrin and that the time at which clotting starts and the type of clot formed are going to be a function of the concentration of fibrinogen in the plasma. Since in whole plasma this reaction is modified by many factors, and since in practice speed and simplicity are essential requirements, no attempt has been made to attain the elegancies which might be considered important by the analytical, physical, or enzyme chemist or by the student of the coagulation mechanism. Rather, the time clotting starts and the character of the clot at 60 seconds after the addition of thrombin are used as

semiquantitative criteria of the concentration of fibrinogen. These observations combined with a knowledge of the patient's status can be most helpful in deciding whether or not one is dealing with a fibrinogenopenia.

Though we have not had extensive experience with this test, we are submitting it for publication at this time because it is so simple and rapid to perform. It gives definitive results at the two extremes of fibrinogen levels, and with our present approximation of the incidence of fibrinogenopenia in this clinic (approximately 1 per 1,000 deliveries) it would take several years to evaluate extensively the actual usefulness of the test. This test, however, has been so helpful to us that we feel others should be allowed to try the procedure so that its value in practice can be more quickly ascertained. This short thrombin test to be described should perhaps be considered as a screening test to be supplemented and complemented by existing testing procedures.

Procedure

Materials and Apparatus Required.—

A bottle or tube containing mixed oxalate (i.e., containing 6 mg. ammonium oxalate and 4 mg. potassium oxalate for 5 ml. blood, such as is used for sedimentation rate or hematocrit and other hematological indices).

Several small test tubes; two 0.2 ml. serological pipettes or two medicine droppers; a watch with a second hand; and a thrombin solution containing 50 National Institutes of Health units of thrombin per cubic centimeter of solution.

This thrombin solution may be made up by weighing out the proper amount of topical thrombin and dissolving it in saline. Originally we weighed out the thrombin into a small test tube which was then tightly stoppered and stored in our special blood bank refrigerator[13] together with another stoppered tube containing the correct volume of saline. The thrombin was then dissolved immediately before use.

More recently the Ortho Research Foundation* has supplied us with small snap-off ampules containing the correct amount of human thrombin ready to be dissolved in saline. Thrombin so packaged may be dissolved by measuring the proper volume of isotonic saline into the ampule with a clean syringe. The needle of the syringe can be used to stir gently to effect solution.

Test Procedure.—

1. Collect 5 ml. of blood in a bottle or tube containing the Wintrobe mixed oxalate (6 mg. ammonium oxalate and 4 mg. potassium oxalate) taking care that *no* clotting occurs.
2. Centrifuge the blood in a clean *dry* test tube or centrifuge tube to obtain plasma (5 minutes is more than sufficient).
3. While the blood is being centrifuged, dissolve the proper amount of thrombin in saline (50 N.I.H. units per milliliter of physiological saline).
4. To test for fibrinogen add 0.2 ml. (or a drop from a medicine dropper) of plasma to the bottom of a small test tube.
5. Add 0.2 ml. (or a drop from another medicine dropper) of the thrombin solution directly upon the plasma, noting the time when the thrombin is added to the nearest second.
6. Immediately mix the two by shaking for less than two seconds.
7. Then, starting with the tube held at an angle of approximately 45 degrees, and in such a way that the bottom end of the tube acts as a pivot, move the other end up and down in the same vertical plane, through an arc of about 45 degrees, at the rate of about 1 oscillation each 2 seconds, so that while the content of the tube remains fluid it flows back and forth along the bottom side of the tube for a distance of about 1 cm.
8. The time clotting starts (if it does) is noted.

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*We wish to thank Dr. H. O. Singher of the Ortho Research Foundation for making these ampules available to us. They will be marketed under the trade name of "Fibrindex."

9. The oscillation of the tube is continued until one is sure the clot formation has definitely started and that it is going to continue.

10. The tube is then held in a vertical position and examined at 30, 45, and 60 seconds by similar single oscillations as were employed earlier.

11. If clotting has not started by 60 seconds, observations are stopped. The test is completed.

Interpretation.—

Plasma from a patient at term with normal fibrinogen levels when tested by this procedure starts to show clot formation at about 5 seconds* after the thrombin has been added. Plasma from a patient with fibrinogenopenia may start to clot at the normal time or may be delayed depending on the fibrinogen concentration and probably other factors. Since the clocking of the exact time of the beginning of clot formation is a function of the trial and also of the observer and since the time may also be a function of other factors such as an increased amount of anticoagulant if enough blood is not originally drawn, estimation of the approximate fibrinogen level must not be made from the time clotting starts alone but must be made from observations of the consistency and character of the clot formed at 30, 45, and 60 seconds as well.

Plasma from a normal patient at term with normal fibrinogen levels will form a firm clot within 60 seconds so that if the test tube is inverted the clot sticks to the glass and very little if any fluid escapes from the clot.

Plasma from a patient with afibrinogenemia or complete absence of fibrinogen forms no clot or fibrin gel at all.

Plasma from a patient with fibrinogenopenia may or may not exhibit clot formation with this test, depending on the extent of the fibrinogen depletion. Those we have observed to date who were considered to require fibrinogen, i.e., with fibrinogen levels at around 100 mg. per cent, have either showed no signs of fibrin formation at all in 60 seconds, or have shown some fibrin formation but no gel formation at all, or gel formation which persisted for less than a few seconds.

No visible fibrin formation is interpreted as a definite indication for the administration of fibrinogen.

A slight tendency to gel formation which tends to contract to a few specks of fibrin, thus leaving within the 60 second period a fluid solution, is also interpreted as a probable indication for fibrinogen.

A definite gel formation, which persists for the minute prescribed with more gel than liquid remaining at the end of the 60 second period is generally interpreted as indicating adequate fibrinogen for hemostasis, though the fibrinogen level might be slightly lower than normal. When the results obtained by this test are equivocal, the observations are best checked by some other means, ideally a quantitative fibrinogen determination. Usually, under such circumstances the patient may be supported adequately with whole blood.

Sources of Error.—

Blood must be drawn without allowing any clot formation to take place. Any suspicion of a clot can lead to serious error. If too little blood is drawn, so that there is too much oxalate, the time of the beginning of clot formation is delayed. However, the clot is usually of essentially normal consistency and appearance at the end of 1 minute.

If the tube in which the reaction is taking place is shaken too vigorously for too long, serious errors will also occur. If there is any doubt, the test had best be run along with a blood specimen from a normal individual. Such a procedure carried out once or twice, preferably before an emergency arises, serves to establish a satisfactory procedure for each observer.

Wet or dirty glassware should not be used.

Old thrombin solution should not be used since in solution the activity of this enzyme is rapidly lost.

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*The average time, as determined by one observer, at which clotting started after the addition of bovine thrombin to 56 plasma samples obtained at random from patients in labor was 6.7 seconds.

Results

In the last nine months 15 blood specimens were submitted to the laboratory to be tested for fibrinogen levels by this thrombin test. Quantitative fibrinogen determinations* were also carried out on these same specimens. The short thrombin test indicated immediately a fibrinogenopenia (i.e., values around 100 mg. per cent or less) in 4 cases. In the remaining 11 the test indicated that the fibrinogen levels were adequate for hemostasis. In all instances the predictions were confirmed by quantitative determination of fibrinogen and by the subsequent clinical course of the patient. These results are shown in Table I.

Normally, we should like to have a larger series of cases before publishing the procedure for such a test. However, based on our experience during the past nine months, we can expect an incidence of about 1 case of fibrinogenopenia in every 1,000 deliveries. Thus, to accumulate a dozen or more cases with hypofibrinogenemia will take approximately three to four years.

In several instances the results obtained by the short thrombin procedure were sufficiently definitive to warrant omission of a quantitative fibrinogen determination. In these cases the subsequent excellent and benign clinical course of the patient serves to substantiate the value of the test.

Comment

The need for a simple, rapid test for fibrinogen to determine approximately the level of this plasma component in a patient with hemorrhage has grown out of the reports of others on fibrinogenopenia and the method of management of patients with hemorrhage instituted in this clinic in 1944, which was described in detail by Cole[13] in 1947 and subsequently by Douglas, Landesman, and Cole.[14] Basically, this management requires that blood lost during a hemorrhage is replaced quantitatively, ideally, minute by minute as rapidly as it is being lost. In the nine years this regimen has been in effect there has been one death from hemorrhage in 43,432 obstetrical discharges and no deaths from hemorrhage in 17,013 gynecological discharges. These results seem to speak well for the regimen established here by Cole. One might even suppose that during this time some few cases of fibrinogenopenia were encountered which were adequately treated with whole blood only.

As knowledge of the syndrome usually described as afibrinogenemia accumulated, however, and as fibrinogen became available to us, we have been obliged to rule out fibrinogenopenia in those cases of hemorrhage in which a deficiency of circulating fibrinogen might occur. It was with this end in mind that this method has been developed.

During the past nine months the test has been in active use and has resulted in our finding those cases of fibrinogenopenia mentioned. As can be seen from the data presented, however, the test was applied between four and five times as often as there were cases of fibrinogenopenia. We expect, as more individuals become acquainted with the test, it will be used even more frequently, possibly

*Quantitative fibrinogen determinations were carried out on the same plasma sample as the thrombin test. Plasma is diluted 10 times. The fibrinogen is converted to fibrin by adding both calcium chloride and thrombin. The fibrin formed is collected and washed in physiological saline; dissolved in 10 per cent sodium hydroxide to which copper sulfate is then added, so that the fibrin concentration is estimated photometrically from the biuret color.

TABLE I

ABSTRACT OF PATIENT'S HISTORY	SEMIQUANTITATIVE TEST INDICATED FIBRINOGEN LOW	QUANTITATIVE FIBRINOGEN (MG. %)	FIBRINOGEN GIVEN (GM.)	WHOLE BLOOD GIVEN (C.C.)	BLOOD GIVEN BEFORE BLOOD DRAWN FOR FIBRINOGEN (C.C.)
1. No. 405456. Admitted with evidence of abruptio placentae with dead fetus. After no progress with conservative therapy of Pitocin stimulation and ruptured membranes, a cesarean section was performed. Bleeding was active but blood replacement equalled output in time and amount. Postoperative course was uneventful	Yes	100	No	3,000	1,000
2. No. 554141. Postpartum hemorrhage of 600 c.c. due to uterine atony, but an otherwise uneventful postpartum course. Returned to hospital 9 days post partum bleeding profusely and a curettage was performed. Bleeding increased and persisted and a hysterectomy was done. Bleeding continued until fibrinogen was given. Postpartum course benign	Yes	125	6	5,500	1,500
3. No. 670837. Admitted with evidence of abruptio placentae with dead fetus. Membranes ruptured and intravenous Pitocin given with cessation of bleeding and subsequent vaginal delivery of 2,240 Gm. deadborn fetus. Postpartum course uneventful	No	230	–	1,000	None
4. No. 613018. Uneventful spontaneous delivery. On fifth postpartum day slight vaginal bleeding occurred and fibrinogen level obtained for base line. Bleeding ceased spontaneously and course continued uneventfully	No	550	–	–	None
5. No. 670854. Admitted with evidence of abruptio placentae with dead fetus. Subsequent delivery by cesarean section of 2,380 Gm. deadborn fetus. Postpartum course uneventful	No	150	–	2,500	None
6. No. 511761. Postpartum hemorrhage on sixth day not controlled by curettage and packing. Total hysterectomy carried out with pathological finding of degenerating decidua and thrombosed sinuses in endometrium. Postoperative course benign	No	440	–	3,000	None
7. No. 656895. Postpartum hemorrhage due to uterine atony subsequently controlled with massage and intravenous Pitocin. Postpartum course uneventful	No	340	–	1,500	Approx. 250 ml.
8. No. 672400. Patient on anticoagulant therapy for 5 days for thrombophlebitis. Vaginal bleeding began fifth day post partum. Controlled with vitamin K. Otherwise uneventful postpartum course	No	340	–	1,000	None

9. No. 673287. Admitted with evidence of partial premature separation with subsequent delivery by cesarean section of 3,160 Gm. living child. Postpartum course uneventful	No	280	–	1,500	None
10. No. 610277. Cesarean section and subtotal hysterectomy performed for premature separation and uterine atony. Postoperatively there continued evidence of intra-abdominal bleeding and shock. An exploratory laparotomy with ligation of active bleeders was done and the postoperative course was benign	No	205	–	6,000	Approx. 3,000
11. No. 625386. Hemorrhage on ninth day post partum not controlled by curettage. Total hysterectomy carried out. Postoperative course benign. Pathological finding of ruptured sinuses of uterine cavity	No	245	–	1,500	None. Two subsequent blood samples show no fibrinogenopenia
12. No. 377714. Para i, gravida ii, Rh negative, immunized with known intrauterine death of one month's duration. Delivered 670 Gm. macerated fetus. Excessive bleeding followed and a curettage was performed. Bleeding continued until after fibrinogen was given and course continued uneventfully	Yes	100	2	1,500	None
13. No. 657695. Admitted with evidence of abruptio placentae with dead fetus. Membranes ruptured and intravenous Pitocin given with cessation of bleeding and subsequent vaginal delivery of 2,880 Gm. dead-born fetus. Postpartum course uneventful	No	375	–	1,500	None

In addition to the obstetrical patients listed above there is one gynecological patient who had two bleeding episodes here with fibrinogenopenia once during an anterior and posterior repair. This case is being described separately as a case report by one of us (W. J. S.).

because of the ease and speed with which it can be performed, the definitive answers it gives at the two extremes of plasma fibrinogen levels, i.e., at very low and high normal levels, and the fact that it can be performed adequately without much practice. We do not recommend that this test supplant any other now in use, however, but that it might be considered as a supplement.

Whenever possible, quantitative fibrinogen determinations are performed also as soon as possible. A quantitative fibrinogen determination can be run in about 90 minutes from the time the blood is drawn. This can be accomplished during the day when the laboratory is open or at other times when one of us (R. W. B.) is available. Even when quantitative fibrinogen determinations are contemplated, this short thrombin test now is run first to give some index of the urgency of performing the quantitative procedure. When clotting starts at about 5 seconds and a firm, solid clot is formed by 60 seconds, a quantitative fibrinogen determination need not be done as an emergency measure; it may be deferred and, as a matter of practical fact, need not be done at all. Thus, unnecessary laboratory procedures are obviated.

Summary

A rapid, simple semiquantitative test for fibrinogen has been described in which thrombin is added to undiluted plasma. The fibrinogen level is estimated from the time clot formation starts and from the consistency and character of the gel formed within 60 seconds of the time the thrombin is added to the plasma. The results obtained with this procedure in 15 cases in which quantitative fibrinogen levels were also determined are presented.

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SORANUS GOES ON AN OBSTETRICAL CONSULTATION AND HOLDS OFFICE HOURS*

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IN THE late thirties a congenial group began weekly meetings in the chaste quiet of the Welch Medical Library of the Johns Hopkins. Those who sat around the long table were Dr. Temkin, Associate Professor of the History of Medicine, Dr. Edelstein, then also an Associate Professor of the History of Medicine and at present Professor of Humanistic Studies in the Faculty of Philosophy, Dr. Eastman, Professor of Obstetrics, and myself. The first two were Greek scholars and Eastman had more than passing knowledge of the language; but I knew not a word of it. Our esoteric task was to translate into English for the first time the Greek text of Soranus. I was the small tail on the large dog, allowed to wag because of a particular interest in sixteenth-century midwifery, founded in large measure upon this second-century work. The task of translating, editing, and interpreting was in such relaxing contrast to the pressure of routine clinical and teaching responsibilities that we selfishly drew it out for a decade. Just now the result of our labor is being readied for publication by the chief worker, Dr. Temkin.

Soranus' name was well known from classical times. For centuries physicians and scholars referred to his opinions with reverence, others quoted paragraphs from his writings with authority. His reputed bibliography was extensive. It included:

A book on the soul;
Ten books on the lives and teachings of the physicians of earlier days;
Works on the pathology and therapeutics of acute and chronic diseases;
A book on the etymology and definition of anatomical and physiological terms;
Practical treatises on: hygiene, pharmacology, and surgery;
A manual on bandaging and fractures;
A book on semen and generation;
Finally, his four books on gynecology.

Until one hundred and twenty-five years ago none of these extensive writings were known to exist except for a brief excerpt from the biography of Hippocrates, and a fragment of the book on bandaging and fractures, both in the original Greek. There was also a fifth-century translation of the work on pathology and therapeutics.

*Presented at a meeting of the New York Obstetrical Society, May 11, 1954.

We might never have known why Soranus was considered the greatest obstetrician-gynecologist of classical antiquity had it not been for 26-year-old Friedrich Reinhold Dietz, Prussian physician-scholar, later Professor and Director of the Koenigsberg Krankenhausen. While exploring the manuscripts of the Bibliothèque Nationale in Paris in the winter of 1830-1831, he came across "codex Parisinus Graecus No. 2153." Codex No. 2153 is a handwritten folio of 517 leaves, each measuring 8½ by 11½ inches.

The volume contains 19 practical medical texts by different physicians with different dates. Judging from the handwritings, scholars believe there were eight copyists, all working about the year 1500. Leaves 218 to 284, penned by a scribe who bears the undistinguished designation of Scribe "E," form one of the 19 books. This is the only book in the volume which "E" copied. One wonders what manner of man he was, was he monk, physician, or scholar? For whom did he copy them? The sixty-six folio Greek pages contain an index, followed by the text of a gynecological treatise without author's name or date. Yet it was not difficult for Dietz to determine that this was the long-lost gynecology of Soranus, for some sections had been copied into other medical texts under Soranus' name and were familiar to Dietz. Actually, his first clue may have come from some unknown reader who had margined one leaf with the notation, "This is Soranus." Dietz died of typhoid when 32, and the work was issued posthumously by an uncritical relative, who published the manuscript as though written in its entirety by Soranus, with the title, *The Remains of Soranus, The Ephesian, on Obstetrics and Women's Diseases.* Scholars soon realized that Dietz's Soranus was a mongrel document made up in large part of Soranus with chapters from sixth-century Aetios of Amida substituted at several points. Furthermore, various anachronistic interpolations had been interspersed by a series of scribes who had made a succession of copies after the original was written, early in the second century A.D.

Ermerins, a Dutch physician, in 1869 attempted a reconstruction. Valentin Rose, a classical philologist, greatly improved the text in 1882. Finally, Johannes Ilberg, also a philologist, after spending nineteen years in purging and editing the garbled Soranus, published his authoritative Greek edition of 1927, the work translated into English by the Hopkins group, under the title, *Soranus' Gynecology.*

The influence of Soranus' book, primarily written for midwives, was great. Muscio, with his famous drawings of the female genitals and the positions of the intrauterine fetus, based his sixth-century Latin obstetrical catechism of 152 questions and answers upon it. The drawings have been handed down from edition to edition and probably stem from antiquity. From Soranus, by the way of Muscio, Rosslin in 1513 derived his German *Rosengarten,* and Raynalde in 1545 his English *Byrth of Mankynde.*

Who was Soranus? All we know is the brief and colorless account left by Suidas, the tenth-century Greek lexicographer, who wrote: "Soranus Ephesus,

the son of Menander and Phoebe, lived for some time in Alexandria, practiced as physician at Rome in the reigns of Trajan and Hadrian, and composed many beautiful books."

After my lengthy prologue, turn back the calendar 1825 years and come to Rome in A.D. 129, the twelfth year of the reign of Hadrian, the most illustrious of Emperors. Together we shall visit the great Soranus and observe him first as obstetrician in the lying-in chamber and later as gynecologist in his doctor's shop.

Dawn came stealthily to the Urbs, city among cities. It was minutes before the first hour of day—night was almost spent and already the sun burnished the horizon. By now Rome's million and a half inhabitants, except for the wealthy who could retire to the depths of their houses, had been awakened by the noises from its maze of streets. The metalworker's hammer blended with the bawling of children on their way to school; the screech of the ungreased axle of the dungcart made weird accompaniment to a baker hawking fresh-made loaves; the chanting cadence of marching soldiers contrasted to the rhythmless grunts of a herd of market-driven pigs.

Paulina opened the shutters and leaned from the window of her fourth floor apartment, gazing down the dim canyon formed by the tall buildings on either side, and the even taller buildings across the Via Jugtarius, a street so narrow that her husband, Lucius Gaius Thoranius, could span it in 5 strides. She mused why the light of dawn came so long after the noise of dawn? In the country whence she had come as a bride the year before, light and noise of the morning kept apace. It had been a long night. She had lighted the wick of tow and wax two or three times to observe the float of the water clock; it had risen so slowly from the tenth to eleventh hour. It was particularly surprising that the hour was so long since this was the summer solstice; at this time the twelve hours of sunlight were much lengthened, while the twelve night hours were proportionately shortened. During that long hour labor had commenced, just when Julia, the hunchbacked midwife, had foretold. She said the babe would knock on the portals of the womb sometime between the Calends and Nones of the month named after the first Great Caesar; here it was the third day of his month. She was glad birthing had begun.

As she stood listening to the cacophony of the world below, Lucius came and put his arm about her. She calmly told him of her commencing accouchement. He was not so calm. Already attired in his tunica, since it served both as bedwear by night and undergarment by day, he tightened the knot in his linen loincloth, wrapped his purple-bordered toga about him, put on his sandals, and raced down the stairs to fetch Julia and her helper, the lesser midwife, Sylvia.

Within half an hour Lucius returned with the women. The hunchback was fighting for breath after the steep flights. She was old, but greatly prized. She could read both Latin and Greek, the latter especially necessary since only in this tongue could one study words of wisdom about the birth process. It was admitted by all that the good physicians of Rome came from

Greece or Egypt. Julia carried a capacious reticule and in it a new book for midwives by the Roman, Soranus from Ephesus. She said when in difficulty she had saved many a baby and mother by simply turning its leaves and determining what the eminent doctor advised. Occasionally in the presence of some special difficulty, when a book did not suffice, she sent for the great man himself. His doctor's shop was in the center of the city, at the edge of the shadow cast in the late afternoon by Titus' Triumphal Arch.

After Lucius had made a morning offering of food and wine to the Lares, his family household gods, the women joined the couple at breakfast. Paulina's childhood nurse, Geta, one of the 50,000 slaves auctioned by Trajan after the second Dacian campaign, served them pomegranates, apples, grapes, bread flavored with salt, cheese, and wine. The talk was lively, hardly reassuring, largely a rehearsal of ghoulish obstetrical happenings the midwives had encountered. After breakfast, they commanded Lucius to leave and remain away. So that Cedric, his slave from barbarous Briton, could fetch him forthwith when the baby came, he listed his itinerary—the barber's, the bookshop, the bath, the forum, finally, the tavern. The helpers, Sylvia and Geta, now eagerly prepared the lying-in chamber. They chose Paulina's bedroom, as it was small, light and air could easily be excluded, too much of either being prejudicial to the laboring and parturient woman.

"Two beds were prepared, one made up softly for rest after delivery, the other hard for lying down during labor, a sagging bed at this time permits the loins to give way" and hinders a baby's progress. They also brought out Paulina's wooden birth stool, used successfully by generations of Rufinas. A moon-shaped cavity of medium size had been cut from its seat "neither too big so that the woman sinks down to the hips, nor, on the contrary too narrow so that the vagina is compressed." The stool had two arms shaped like the Greek letter *Pi*, providing a "crossbar on which to press the hands in straining." Behind there was a straight back "so that both the loins and hips may resist any gradual slipping," for if the laboring woman is allowed to assume a "crooked position, it hinders descent of the fetus."

Meanwhile midwife and patient paced the floor, pausing frequently for Paulina to squat over the silver chamber pot. At first the throes were mild and infrequent, but by the fifth hour of the sun they were strong, often, and painful. Paulina was tired and asked to be allowed to rest. She was led to the firm bed and instructed to lie flat on her back, ankles touching, thighs separated. A hard pillow beneath her back inclined the vagina downward. At first, the midwives soothed the pains by putting their warm hands over her belly and loins. Later they soaked pieces of cloth in warm olive oil, fomenting her abdomen and labia, while on either side they placed pigs' bladders filled with hot oil. Paulina appreciated the kind attentions, but was confused as to why in midday July all medication had to be *hot,* when cold would have been far more agreeable. Julia explained that heat relaxes, and opens up the constricted parts, while cold contracts and closes them.

The midwife decided to examine her. First she removed the woolen modesty cloth which discreetly covered her privy parts and, by means of a

sponge, cleansed the region with water. Then anointing her hands with oil she inserted the forefinger of her left hand, the digit with the closely pared nail, into the orfice of the womb and attempted to dilate it gently and gradually so that more and more of the accessible part of the membranes would bulge forth. With her right hand, meantime, she anointed the vagina, making certain the oil had not previously been used in cooking.

Much to the widwife's distress, attempts to dilate the orifice resulted only in unrewarding pain. Paulina read apprehension in the mobile features of the hunchback and sobbed with fright and wretchedness. The two midwives tried to reassure her, promising that by the tenth hour of day a baby would be in her arms. They offered her mushrooms, a squab, and fruit, but all the appetites of her body had been driven out by the pain. They coaxed her to walk again, hoping the baby would force its way lower and stretch the orifice. At this juncture Lucius returned, apologizing for not waiting until sent for, but he was worried by the passage of so many hours. His obvious anxiety could not temper Paulina's fears so the midwives barred him from the lying-in chamber.

Going into the atrium he stood before the Lares, the household gods of his family. Previously when he talked to them they listened, even answering his words. He prayed, "If it please you, oh, Lares, may Paulina soon have happy and safe deliverance." Today they did not hear, faces of stone stared back in silence, and Lucius interpreted their silence as an evil augury. He opened the cupboard containing the wax masks of his ancestors; the masks dated back to the time of the Civil War when the Thoranius family first became important. He took solace in the thought that all these men and women had been born successfully and in turn all except Fluvius and Plotina had progeny. His reveries were interrupted by a shrill cry from the labor room. Beside himself, he intercepted Geta coming back from the kitchen and asked her to summon Julia.

Lucius, already a centurion, young as he was, commanded one midwife as vigorously as his company of 100. He told her he was determined to call the physician Soranus and dispatched Cedric for him. Night had fallen. Lucius ordered the lamps lighted, lamps made of bronze and copper, some shaped like boats, others, flowers, and still others, animals. They were all about the apartment. In the atrium there was an ornate iron candelabrum from which hung six lamps shaped like doves. Lucius looking upon the scene below beheld a procession wending down the middle of the narrow street. Cedric was followed by two tall torchbearers with girded swords, then four Nubian slaves supporting a litter. The company stopped at the door. In a moment Soranus stood before him; a slave followed carrying a leather bag.

Soranus was of average height, with thinning gray hair, but his perfumed, full beard, cut in the manner of the Emperor's, was dark. Penetrating black eyes were his most prominent feature. He was attired in a fine-spun toga, artfully draped about his broad torso in a self-conscious tumult of folds. Several fingers were circled by heavy gold rings, some set with precious stones.

He greeted Lucius, and in a very efficient manner asked Julia about the course of labor and why the baby was so stubborn in issuing forth. She said perhaps the pubic bones had unhappily grown together and fused into a solid joint as is their wont in men. Then mayhap the neck of the uterus was bent and the force of the fetus' birth efforts were not directed against the os but anterior to it. While listening attentively Soranus gave the rings to his slave. His only comment was, "Even if one loses the infant, it is more important to take care of the mother. I hope to save them both." He bade Julia conduct him to Paulina.

When he entered the lying-in chamber his cheerful bulk filled the room with confidence and hope; for the first time in many hours Paulina smiled. He bade her lie upon the firm bed, felt her tunic-covered abdomen and queried the midwives about the urine and bowels. When told she had voided only a few drops at a time he asked for his bag, took out a silver catheter, and beneath the chaperonage of the cover, deftly passed it by means of a keenly developed sense of touch. The water drained forth in a continuous interminable stream as from a leak in the aqueduct. Soranus retired and ordered the midwives to administer an enema of warm water, olive oil, and honey. After this, the pains were more more frequent and stronger, but Paulina stood them better. Either they hurt less or the presence in the next room of the great physician made them more bearable.

The patient was advised to get up and walk. She and the midwives noticed that the top of the womb which had pressed sorely under her ribs had descended and there was now a space of several fingers above it. All were encouraged. At Soranus' insistence Paulina rekindled her strength with bread, liquid barley gruel, and a small slice of melon.

Paulina was put back to bed, properly covered, and prepared for examination. While the physician anointed his left hand with warm oil (the left is softer than the right and can be introduced with greater delicacy) a midwife poured the whites of several eggs into the birth passage. Introducing his anointed hand, the nails being pared so they would not scratch, Soranus thoroughly churned the vagina with the slippery foaming albumin. Attempts to rupture the chorion with the finger were unsuccessful so it was incised by the point of a scalpel. A little clear fluid drained forth. Forming fingers into a cone by extending them and joining the tips together, he passed them through the cervical os while dilated by a pain. The whole company stood transfixed; they marveled at the great doctor's gentleness and assurance. Paulina was fascinated. Sensing the interest of the spectators, Soranus began to speak: "I can feel the hand and arm of the babe thrust out in front of the head. One must not sieze the hand and pull; this would render the impaction worse. I shall place my finger tips against the head, raising it up into the cavity of the uterus and then push on the shoulder thus raising up the whole fetus." With the onset of a contraction he stopped both the explanation and upward pressure. When the contraction had passed, he resumed his work. A moment later, apparently satisfied, he withdrew his hand and said,

"Paulina, now all will be well. I succeeded in pushing the hand up into the womb by bending the elbow. I then placed the hand alongside the baby's thigh so that it may no longer hinder delivery, and grasping the baby's head, I gently drew it into position. I, Soranus the Ephesian, promise you will be delivered before the night watch has twice made its rounds."

He left followed by Lucius who asked the fee; when told two aurei, three were given to the slave for his master. Lucius wished Soranus to remain but he refused, saying he was no longer necessary, yet would hold himself in readiness. Lucius promised to send Cedric to tell him as soon as birth occurred.

With delivery so imminent Julia said that a third helper was needed. Despite the late hour, Lucius went to a neighboring apartment and brought back Flavia, Paulina's best friend. Paulina was placed on the birth stool, rubbed with warm oil, given a vaginal instillation of the same substance, and her feet covered by a blanket; all of these measures to prevent chilling at so susceptible a time. Flavia was stationed on the left of the birth stool, Geta on the right, and Sylvia behind. Taking her position in front of Paulina, Julia instructed her how to strain down by grasping the crossbar on either arm of the stool, then to drive her breath into the flanks without screaming; this by retaining the breath and groaning at the same time. She was exhorted not to give in to her pains but to strain the most when they were present. They loosened her girdle and undid the breast binder so that her breath might pass unhindered.

Julia covered herself with an apron and sat on a low stool directly in front of her patient, legs parted, the left a little in front of the right, to make it easier to work with the left hand. Having read in Soranus "that the midwife should beware of fixing her gaze steadfastly on the genitals of the laboring woman, lest being ashamed her body become contracted" she looked fixedly at Paulina's young and goddesslike face. Between pains, it was relaxed, smooth, and pale; but with the straining it became distorted, furrowed, and scarlet. At each throe, both the friend and slave restrained her on the birth stool, while the lesser midwife fixed her rigidly against its back. Julia with a circular movement of her anointed fingers dilated the labia and the orifice of the uterus. When the head had descended she inserted her fingers and gently pulled the embryo forward, letting it retreat after the pain had passed. The helpers on either side pressed the belly downward toward the lower parts and at the same time Sylvia crouched down and, from her position in back, supported the anus with a pledget to prevent it from prolapsing.

As the head was born, Julia covered her hands with pieces of cloth so that the infant would neither slip nor be squeezed, and, as Paulina strained down, she drew it forth. The child, a boy, cried at once. No lyre played by the goddess of music would have sounded half so sweet.

Julia handed the babe with cord still attached to a helper. Guided by the cord, she inserted her hand into the uterus and, while the parturient strained, gently removed the placenta by lateral movements, neither rending nor tearing it.

They grasped Paulina under either arm and half led, half carried her to the bed previously prepared. She sank into it with grateful fatigue; closing her eyes she gave a silent prayer of thanks to Lucina, the goddess of childbirth.

After the baby had rested a little from the agitation caused by birth, Julia performed the oldest operation yet known, omphalotomy. She cut the naval cord with a knife, four fingerbreadths from the abdomen. After squeezing out the coagulated blood which its vessels contained, she ligated it tightly with a twisted piece of wool. Before bathing the baby, they brought him to his mother, so that she could hold him in her arms. As she did so, Lucius tiptoed in and through a mist of joyful tears hazily saw his squirming son. He quickly remembered that he was a centurion and, ashamed of his womanish weakness, withdrew.

As Cedric was dispatched to Soranus with the good tidings, the sun was fighting its way over the horizon to signal yet another day. Lucius went into the atrium and crowned the Lares with garlands of myrtle which the servants had brought. In immense gratitude, he spread before the gods a feast of cake, honey, and wine; as a special mark of thankfulness, a roasted pig also. He said "I, Lucius Gaius Thoranius, thank you, oh, Lares, for answering my prayer and granting Paulina a happy and safe deliverance. And extra thanks because it was a boy, another soldier for my Emperor's armies." This time the Lares heard, this time the Lares smiled.

Soranus' doctor's shop is on the ground floor of a large apartment house. Being on the ground floor has several advantages, foremost, a conduit from the aqueduct provides fresh running water; then, too, a first-floor location allows passersby to stop and purchase drugs or cosmetics. His cough lozenges for children from small pine cones, roasted almonds, linseed, the juice of licorice, tragacanth, and honey are much in demand. The efficacy and variety of his contraceptive prescriptions are known to all ladies of quality. Two of the more popular: Rub an equal quantity of the inner bark of the pine tree with tanning juice and wine, steep some wool in it, insert the wool as a tampon, remove after two or three hours, and have intercourse. The second: Of unripe oak galls, of the inside of pomegranate peel, and of ginger, each two drams, mold with wine to the size of vetch-peas, dry indoors, and insert as a pessary before coitus. He advises some customers in addition, as a precautionary measure, to drink Cyrenaic* balm once a month to the amount of a chick-pea in two and a half ounces of water; this potion encourages menstruation. On the other hand, if the menses are very recalcitrant and fail to appear, he has available another prescription: Thirty grains of wallflower seed and of myrtle, a drachm of myrrh, two seeds of white pepper, all dissolved in wine, to be drunk on three successive days.

The shop is situated between a hairdresser and jeweler. Several physicians are located on the same block, among them Archigenes, the famous surgeon, and Aspasia, the illustrious obstetrix, female obstetrician.

*An aromatic lotion from Cyrene, a Greek city in Africa.

The front room is large with its street side almost completely shuttered; when opened it is airy and light. There are counters and shelves, baskets and urns, all containing common and rare drugs properly labeled, some raw, others mixed and already compounded. Three walls are lined by cushioned benches. In the rear are two rooms, one an office in which Soranus sees patients, in the other he mixes special prescriptions too complex even for his experienced servants.

On a low three-legged table in his own sanctum the bronze and lead tools of the trade are arrayed. There are vaginal and rectal specula, some tubular, some with a single blade, others with two or three blades. There are scalpels—blunt and sharp pointed, sounds and probes of all lengths and varieties, including graduated cervical dilators. There is a special row of surgical forceps—narrow, broad, toothed, and plain. There are perforated irrigating tubes, catheters, and elaborate stoves with spouts for the fumigation of body orifices. His special obstetrical armamentarium consists of hooks and large knifelike embryotomes for destructive operations on the fetus.

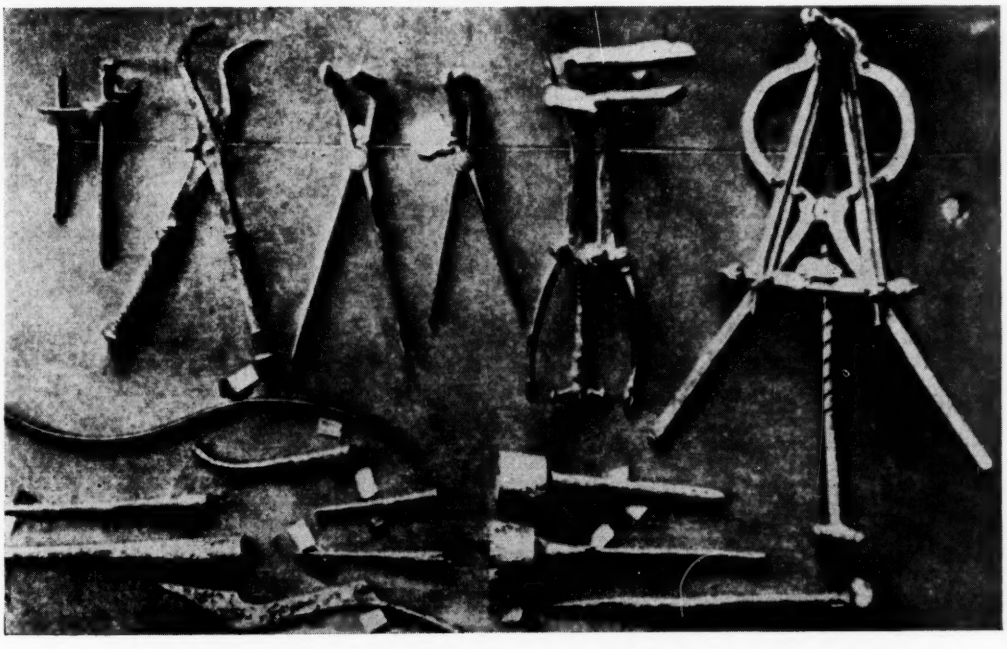

Fig. 1.—Gynecologic instruments unearthed at Pompeii—specula, catheters, douche nozzles, etc.—buried by lava and ash in 79 A.D., sixty years before our story. (From Ricci: The Development of Gynaecological Surgery and Instruments.)

The rest of the office furniture is quite simple: one large chair with sloping back, a couch, and several stools, a heavily padlocked chest, and a handsome gold caduceus ornamenting the top of a water-clock. In one corner a dolphin-shaped spigot projects from the wall above a marble washbasin.

As we enter the shop we find the waiting room peopled with all manner of persons: freedmen, citizens and senators, women and children. A patient holds a cloth over his eye, another a poultice to his swollen jaw, and a third, a

woman, lies on a mat on the floor. When we go into the inner office we find Soranus sitting in his chair with four pupils ringed behind, three very young men and a woman somewhat older, perhaps thirty. Two servants, a man and woman, stand at the far end of the room with eyes fixed on their master, prepared to anticipate his bidding.

Since my paper is already long, I shall content myself with reporting the first two gynecological cases, omitting the medical, surgical, and orthopedic sandwiched between.

The first is a very beautiful young matron. It is likely from her many-tiered coiffure, her rings and bracelets, her heavy, exotic perfume, and her vivid-colored palla fashioned from China silk, that she is the wife of a member of the Court.

Soranus is saying:

"Sabina, your failure to conceive may be related to the time of the month you have intercourse. Just as every season of the year is not favorable for sewing seed to grow grain, so not every time is suitable for sewing the seed discharged during intercourse. The best time for fruitful coitus is when menstruation is ending and abating. The time just before menstruation is sterile because the uterus is already overburdened; the overburdened stomach is similarly averse to receiving food. The truly propitious time for coitus is during the waning of the menses, for then the uterus has been lightened, and it has warmth and moisture just in right measure. Its cavity has been recently roughened by menstruation so that the semen of both the man and woman is safely retained and adheres. Even if a few women have conceived at other times in the month one must not pay attention to their success for it is more profitable to point out the proper time as determined purely from the theory of our art.

"Further advice for you may be unnecessary, but when discussing barrenness, no knowledge can be taken for granted. A wife cannot hope to conceive unless the urge and appetite for intercourse are present. Just as food swallowed without appetite and with aversion cannot be well received and digested, so neither can the seed be taken up and grasped unless there is the urge and appetite for intercourse. Although some women who have been raped conceived, one may be certain that sexual appetite existed in them too, but was obscured by strong mental resolve.

"There is more to say, but I shall be brief. To conceive, the body must not be overloaded with food nor depleted from its lack. Above all there must be no drunkenness. Just as the union of a wound is made difficult by the vigorous rising up of a gross superfluity of wine, so the attachment of the seed is even more disturbed by it."

One of the students interrupts, "Master, I have heard that environmental factors influence the ease of conception. Is this true?"

Soranus answers:

"Some of the ancients have written that the proper time for conceiving is determined in large measure by external factors. Thus the time of the waxing

moon has been deemed propitious, for things down on earth are believed to be in sympathy with things up above. In house mice, the lobes of the liver are supposed to increase with the waxing moon, but to decrease with its waning. Furthermore, these same authors state that Spring is the supreme season for conception. Without submitting either the lunar or seasonal thesis to philosophical analysis, we may dismiss each for we see successful pregnancies beginning at all phases of the moon and in all seasons, with no apparent calendar preference.

"Sabina, in my eagerness to teach I almost forgot you. Practice what we have said, and if you have not conceived by the time of the equinox, return. Give my salutations to the Emperor and to Sempronius, your husband."

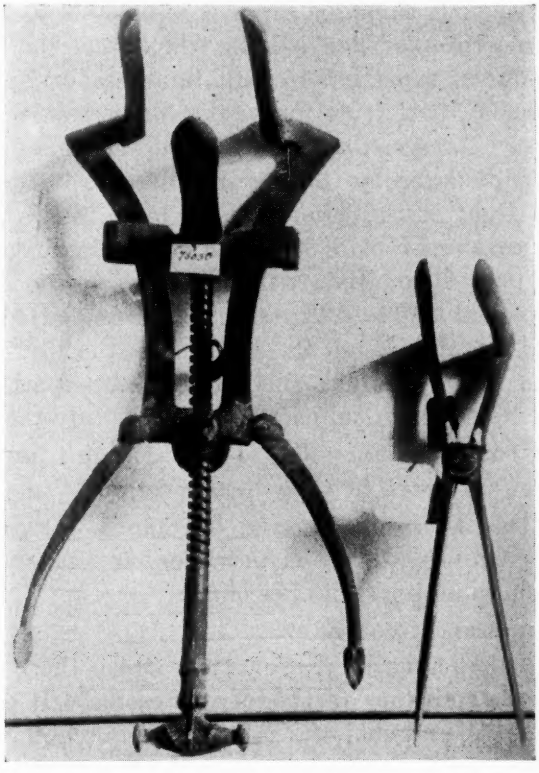

Fig. 2.—Bivalve and trivalve vaginal specula unearthed at Pompeii. Date from first century A.D. (From Ricci: The Development of Gynaecological Surgery and Instruments.)

"Thank you, master. I shall take heed. I always feel better when ill, and encouraged when depressed, after seeing you." With these words and a radiant smile, Sabina withdrew leaving her perfumed fragrance behind her.

The second gynecological patient we saw lying on the mat. Wasted and cachetic she enters carried in the arms of a stalwart son. The servant motions toward the couch; the rough, bumpkinish peasant deposits her with the most exquisite care.

Soranus asks "Mother, what ails thee?"

She tells her story in a torrent of anguished words with a provincial accent that marks her as coming from distant Sicily. She stated that a vaginal flux appeared over a year ago which soon became bloody and has been unremitting since. Soranus asks her age. Her only reply is that her oldest child was born while Domitian was still the Emperor.

Soranus signals the female servant to prepare the patient for examination. In the meantime he gathers the students in a tight knot about him.

He begins to discourse:

"Hemorrhage of the uterus results from difficult labor, miscarriage, erosion by ulceration, a porous condition, or from the bursting of blood vessels. Its presence is clearly recognized from the sudden and excessive rush of blood; besides, the patient becomes weak, shrunken, thin, pale, and when it persists, anorexic. It is a grievous calamity for it is impossible to stop it by pressure with the fingers, insertion of hooks with which to twist the blood vessels, plugging with pledgets, constriction with ligatures or by stitching with a suture. The blood may flow from the vagina or uterus, the distinction must be made by the use of a speculum. Treatment depends on what is found." He punctuated his discussion by leading the students to the couch which had been drawn to the light of the window. His back to the window, a servant hands him a lubricated two-bladed speculum which he gently inserts. He works quickly, deftly, confidently; with a piece of cotton held in a long forceps he wipes away the blood and exposes a huge, eroded, ulcerated mass. He attempts to pass a sound through its center into the uterus, but the way is blocked. Removing the speculum, the servant, anticipating his next move, hands him a suppository which he inserts and packs into the vagina. He says:

"Now mother, that is all for today, I hope I didn't hurt you. Send your daughter in later, I want to tell her how to care for you."

Soranus went to the basin, washed his hands, scraped them with the strigil, dried, and perfumed them. Meanwhile, her son tenderly picks up the frail little woman and mutely carries her out.

Soranus continues his discourse:

"You observed that huge ulceration from which there is active bleeding. I inserted a drastic suppository to produce an eschar. It contained oak gall, pulverized frankincense, and chalcites in equal parts together with sweet wine. In addition one must place the patient on a strict regimen of which we shall speak another day."

A student inquires, "Good master, why did you not practice bloodletting in this case as Themison recommends, to divert the blood away from the part which is bleeding?"

Soranus answers: "In cases of hemorrhage we reject bloodletting, for bloodletting relaxes whereas hemorrhage demands condensation and contraction. One's goal must not be to divert blood but to stop it. Venisection may be critically dangerous since, if the flow of blood is not checked by it, the patient necessarily succumbs more quickly, being exhausted by a double hemorrhage, as it were."

As a tear-stained child, guardedly supporting a broken arm, is lead in from the waiting room we leave the great physician still immersed in work.

I hope this fanciful, but meticulously documented essay has given you a feeling for Soranus, his medicine, and his times.

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A MICROELECTRODE METHOD IN THE DIAGNOSIS OF CARCINOMA OF THE CERVIX AND ENDOMETRIUM*†

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TESTS for the presence of cancer are not yet so satisfactory that any new approach can be neglected. Histological and cytological indices are not always decisive and are not easily accelerated to give an answer during an operation. Chemical determinations on blood or urine, while steadily improving, do not yet give fully reliable results. The methods of diagnosis of carcinoma of the female generative tract are histological and cytological. Microscopic examination of tissue is informative when there is a target lesion or when serial sections are studied; but this is generally not practical. The cytological method (Papanicolaou) is accepted as a screening method but it is not definitive, and histologic confirmation is required before a final diagnosis is made.[3, 4, 9] The ultimate goal sought is the diagnosis of cancer cells before their invasion of the host. The present paper is a report on the application of the newer bioelectric techniques to the measurement of the membrane potential of cancer and related cells. Experiments so far have been limited to the female genital tract. Results are encouraging, but this report is still preliminary.

Single cells can be impaled with a microelectrode and the potential across the membrane measured by comparison with an external electrode. This method, applied especially to many types of nerve and muscle cells, has revealed potentials of as much as 100 millivolts, outside positive to inside.[2, 6] Since these potentials, further, vary with the metabolic state and the ionic balance between cell and environment,[2, 5, 7] it seemed possible that malignant cells would differ from their normal counterparts in size and behavior of the membrane potential. Although our limited findings do suggest a lowered membrane potential in cancer cells, a potential picture in the cells of a vaginal smear which is different in normal and malignant cases, has led to promising results in cases of uterine cancer. These findings form the basis of the present paper.

Methods

The microelectrode technique of Ling and Gerard[6] was applied to isolated tissues of the female genital tract and to vaginal desquamation. The technique

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†Presented at a meeting of the Chicago Gynecological Society, May 21, 1954.

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consists of inserting, with the aid of a micromanipulator, a potassium chloride-filled glass needle with tip diameter less than 0.5μ, into individual cells, picked at random. The membrane potential, measured as the potential difference between the internal electrode and an indifferent electrode in the bathing solution, is recorded by means of a cathode follower leading into a wall galvanometer (Fig. 1). A voltage calibrator is included in the circuit and used with the microelectrode inside the cell.

The electrodes were drawn by hand from 1.5 mm. tubing in a small oxygen flame. Filling with 3 M. KCl was accomplished by inserting into the shank end another capillary, with broken tip, pushing it home into the tip, and forcing out the fluid by a syringe connected by polyethylene tubing. The fluid fills the tip automatically, by capillarity. Each electrode was examined microscopically to be certain that filling was complete and then sealed into a KCl-filled tube, held by the micromanipulator.

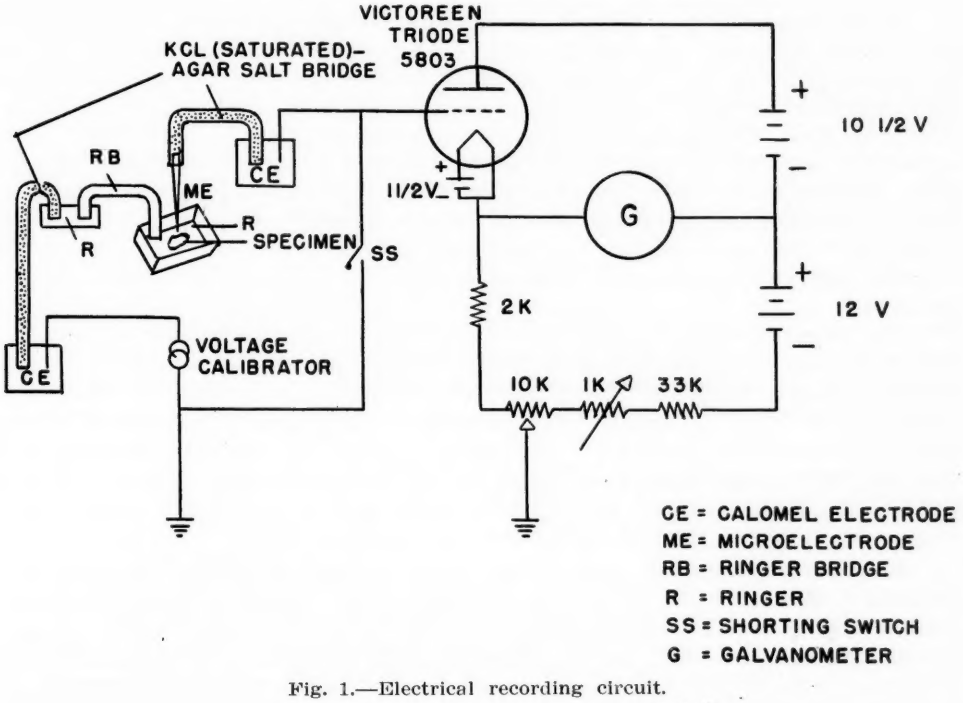

Fig. 1.—Electrical recording circuit.

In use, the electrode position was observed under a binocular microscope. A successful impalement is indicated by a rapid galvanometer deflection, the maximum being the reading. A convenient sensitivity, set by means of the galvanometer shunting resistance, is 2 millivolts per centimeter deflection. Different regions of the sample are explored with the electrode so as to ensure a random sampling of the cell population. It is desirable to have a sample layer of at least 0.5 mm. thickness, to avoid contact between the electrode and the bottom of the chamber and consequent electrode breakage or artifact potentials.

The materials examined included intact mucosa from freshly excised uteri and vaginas, and exfoliated cells contained in vaginal secretions. Tissue, obtained at operation or by punch biopsy, was oxygenated in mammalian Ringer's solution within 20 minutes after removal. Representative vaginal contents were obtained by inserting a vaginal speculum, withdrawing it, and

transferring the contents with a small spatula to the chamber. As will become clear, it is important that the vaginal specimen represent exfoliated cells; hence the cervical mucosa must not be scraped nor the vaginal contents swabbed prior to obtaining of a specimen. Generally 20 to 25 cells were measured, in 10 to 15 minutes, at room temperature, to obtain a spectrum of the cell population. Samples will keep for at least 24 hours in the cold without deterioration.

Possible difficulties, which could lead to spurious results, are: A broken needle, which cannot successfully penetrate the cell, may give low or erratic values, not interpretable. Vaginal cells have a high resistance and, occasionally, with the electrode inside the cell, some instability in reading results. This could give a false impression of the direction of membrane polarity; and, for this reason, it is wise to calibrate with the electrode inside the cell.

Results

Nonmalignant tissue was obtained from patients undergoing hysterectomy for uterine fibroids. Malignant specimens were from patients with primary carcinoma of the cervix, two untreated and one recurrent, obtained at hysterectomy or by punch biopsy. Normal (i.e., nonmalignant) endocervix cells averaged 33 millivolts positive (outside positive to inside) while the potentials of cells of carcinomatous cervix were considerably lower, 22 millivolts positive on the average (five normal cases, total range of cells 30 to 48; three malignant cases, range 19 to 27). Normal endometrial cells range widely but tend to be similar to or lower than those of normal endocervix, and vaginal cells also averaged 30 millivolts, as did those from the squamocolumnar junction.

Early in the study it was noted that cells in vaginal secretions from nonmalignant cases exhibited predominantly inverted potentials, with the outside negative, rather than the positive orientation of most body cells, while those in secretions from malignant cases showed mainly the normal positive potentials. The negative cells were primarily vaginal and the shift in malignancy was interpreted to mean that many more intact cells than normal, of endometrial or cervical origin, were desquamated and found in the vaginal secretions. A number of other facts support this interpretation.

1. The desquamated and dying cells of smears normally show lower potentials than those in the live epithelium, with vaginal cells constituting at least two-thirds of the total (Table I). In malignancy, the negative vaginal cells constitute less than half of the total and the remainder is of endometrial cells with a potential, +10 to +30, much closer to the normal endometrial cells in situ. The early and profuse shedding of more viable uterine cells in malignancy would fit this picture.

2. Malignant cells do shed more easily than normal.[1]

3. After total hysterectomy no cells with positive potentials are found.

4. During normal menses (but not in pregnancy), cells of the uterine type, +4 to +10 millivolts, suddenly constitute up to 100 per cent of the total.

To recapitulate, malignant cells exfoliate in greater numbers, as indicated by the larger proportion of cells of uterine derivation found in vaginal desquamation, and further, exfoliate in a more viable state, as indicated by the larger potentials of such cells, which may approach those of intact tissue. It deserves note that these conclusions, arrived at de novo on the basis of electrical measurements, are entirely consistent with and supplement findings based upon other methods.[1]

Aside from any physiological significance of these findings, the results suggest a possible diagnostic test of pathological exfoliation. Thus far, it

appears that the conditions in which this has been found to occur, besides menstruation, are malignancy and some endocrine disorders, notably hyperestrogenism.

TABLE I. POTENTIALS OF DESQUAMATED CELLS

CASES		PER CENT OF ALL CELLS SHOWING POSITIVE POTENTIALS	POTENTIAL RANGE	
			POSITIVE mV.	NEGATIVE mV.
Malignant (18)				
Invasive	(16)	55-100	10-30	-3 to -40
In situ	(2)	54-57	2-8	-3 to -28
Nonmalignant (38)				
*Normal	(32)	0-32	2-8	-6 to -80
Pregnancy	(3)	0-31	2-4	-6 to -88
Menstrual	(3)	22-100	4-10	-6 to -40

*Includes mainly patients with varying pelvic complaints plus some normal volunteers, as well as 6 patients with past history of carcinoma of cervix successfully treated by radiation or hysterectomy.

The technique has been applied to the diagnosis of cancer of the cervix in 58 cases (Table II). Twenty positive diagnoses were made, of which 18 were correct. Two represented carcinoma in situ, 2 were clinically Stage I, and 7 were recurrences, of which 3, previously unsuspected clinically, were confirmed by biopsy or operation. One of the false positives was associated with endocrine bleeding and was negative on a later recheck. Carcinoma in situ showed, in the 2 cases studied, a combination of normal and abnormal findings. The proportion of desquamated cells of endometrial origin was much higher than normal, but their potentials were in the normal range of +2 to +8. In addition, the magnitude of the negative potentials was lower than normal with only few cells in excess of –20 millivolts. A case with metastases to the vaginal vault at the line of suture, 8 months following removal of the uterus by a Wertheim operation, was, surprisingly, one of the correct positive diagnoses.

TABLE II. ANALYSIS OF DIAGNOSTIC RESULTS

DIAGNOSIS	NO. OF CASES
Correct positive	18
Correct negative	35
False negative	0
False positive	2
Normal menstrual	3
Total	58

Thirty-five negative diagnoses were all correct. Twenty-five were on patients admitted to the gynecological ward or to the outpatient clinic in order to rule out carcinoma, and 4 of these cases were first diagnosed clinically as probable carcinoma but later proved negative by biopsy or operation. The test does not appear to be complicated by pregnancy; 3 women between the sixth week and the seventh month of pregnancy gave normal smears.

Of the 57 cases, 14 were checked with the cytological technique of Papanicolaou. In all cases (13 negative, 1 positive), the two sets of results were in agreement.

One smear was studied which did not fit any of the patterns described. Results are not included in the tabulations since the patient did not return for a final diagnosis. Repeated Papanicolaou smears had been reported as Class II and Class III, with the frequent comment, "Possibly malignant." Electrical measurements indicated typical malignancy except that the positive potentials

were higher than in malignant desquamated cells and well in the normal range of intact endometrium or cervix. The potential picture suggests active exfoliation, but from a nonmalignant site. Whether this represents a precancerous or a benign condition deserves investigation.

A final caution is in order. Dr. Geraldine Kiebel, who has repeated these studies semi-independently during the past year, has not obtained as consistent results. Nevertheless, in a series of significant findings the results have been: True positive 10, false positive 4, true negative 30, false negative 0. Thus, no false negatives have been encountered to date and the false positives have occurred in 6 per cent of the normals in the first series, 10 per cent of the later one.

Summary

1. A method is presented for measuring the membrane potentials of tissues and desquamation of the female generative tract.

2. It is possible to distinguish desquamated uterine from vaginal cells, by the inverted polarity of the latter; and prematurely desquamated cells by their larger potentials than those of old cells desquamated normally.

3. In uterine carcinoma, the percentage of uterine to vaginal cells is increased in smears and many are desquamated earlier, as judged by the potential picture.

4. The potential measurements on smears have yielded no clinically confirmed false negatives, 5 to 10 per cent false positives.

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LIPOMATOUS TUMORS OF THE UTERUS

A Review of the World's Literature With Report of a Case of True Lipoma

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FATTY tumors of the uterus are rare. They have been divided into true or pure lipomas and mixed lipomas (fibromyolipomas, myolipomas, and fibrolipomas). Their rarity prompted us to report this case which is the second one from the Jefferson Medical College Hospital.[16] We have compiled the world literature and analyzed these tumors in regard to the age of the patient, associated symptoms, location of the tumor, and the different theories of histogenesis.

Incidence

Lobstein,[39] in 1816, recorded the first case of a fatty tumor in the uterus. Stroinski,[71] in 1880, described a pure lipoma of the cervix.

Following a complete survey of the literature, 33 cases of pure lipomas (Table I) and 63 cases of mixed fatty tumors (Table II) have been found. All of the true lipomas have had histological diagnoses. The diagnosis of a few of the mixed tumors have not been substantiated histologically, but the gross description warranted a diagnosis of fatty tumors and they have been included for the sake of completeness.[37, 39, 51, 63]

Age

Of the true lipomas where the ages of the patients have been recorded (27 cases), 67 per cent were between the ages of 50 and 70 years. Eleven per cent were beyond 70 years, 11 per cent between 40 and 50 years, and 11 per cent under 40 years of age. The youngest woman was 28 and the oldest was 78.

Of the mixed lipomas where the ages were reported (48 cases) about 80 per cent of the tumors occurred in patients between the ages of 50 and 70 years, 2 per cent beyond 70 years, 9 per cent between 40 and 50 years, and 9 per cent below 40 years. The youngest patient was 23 and the oldest was 81 years.

These figures show that fatty tumors of the uterus primarily occur in elderly, postmenopausal women, particularly among those in the sixth and seventh decades.

Etiology

There are many theories concerning the histogenesis of these tumors. Briefly they may be listed as follows:

1. Misplaced embryonic fat cells.[3, 5, 14, 15, 22, 28, 32, 34, 42, 43, 49, 53, 54, 57, 64, 65]
2. Metaplasia of muscle cells into fat cells.[8, 11, 19, 27, 40]
3. Metaplasia of connective tissue into fat cells.[18, 19, 29, 38]
4. Lipocytic differentiation of a specific primitive connective-tissue cell.[70]

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TABLE I. TRUE LIPOMAS

AUTHOR	AGE	LOCATION	SYMPTOMS	THEORY OF HISTOGENESIS
1. Stroinski	28	Anterior lip of cervix	—	—
2. Merkel	—	Interstitial near right cornu	—	Misplaced embryonic cells along Wolffian duct
3. Meyer	42	Posterior, subserous near cornu	—	Misplaced embryonic cells
4. Ellis	60	Anterior, interstitial in corpus	—	—
5. Kauffman	47	Posterior in corpus	Abdominal pain, bleeding	Metaplasia of connective tissue
6. Elkin and Haythorn	46	Submucous, posterior wall	Bleeding, abdominal enlargement	Misplaced lipoblastic cells
7. Schleussner	60	Posterior, interstitial in corpus	Pain	—
8. Pulsch				
9. Askanazy	65	Interstitial	—	Misplaced embryonal cells
10. Dworzak	75	Posterior, left cornu	—	Misplaced embryonal cells
11. Thaler I	65	Interstitial, right side in corpus	Abdominal distention	—
II	—	Interstitial, right side in corpus	—	—
12. Glas	60	Anterior, interstitial in corpus	Abdominal pain	Fat accompanying vessels
13. Lund	71	Corpus	Tenderness	—
14. Muschik	56	Posterior in corpus	Bleeding	Misplaced embryonal cells
15. Keller	63	Anterior, interstitial and right corpus	Bleeding, abdominal enlargement	—
16. Nordin	59	Corpus	Bleeding	—
17. Burger	67	Subserous, anterior, and corpus	Abdominal pain, backache	—
18. Hall	63	Interstitial, corpus	Bleeding, pain	—
19. Ritter and Stringer	57	Anterior	Bloody discharge, backache	—
20. Kaseman	62	Interstitial, left corpus	Abdominal pain and fullness	Misplaced embryonal cells
21. Reich and Necktow	39	Corpus	Abdominal enlargement	—
22. Sivo	—	—		
23. Ikonomou	61	Interstitial, right and anterior corpus	—	—
24. Howe and Kellert	60	Corpus	Spotting, backache	—
25. Palla	59	Posterior, corpus	Abdominal pain	—

TABLE I—CONT'D

AUTHOR	AGE	LOCATION	SYMPTOMS	THEORY OF HISTOGENESIS
26. Wirtz and Oliviers	60	Corpus	Pressure, heaviness	—
27. Decker	50	Right cornu	Descensus	—
28. Henriksen I	39	Left cornu	Abdominal pressure	Misplaced embryonal cells
II	69	Posterior corpus	—	
III	68	Posterior corpus		
29. Kovats	—	—	—	—
30. Abrescia	78	Posterior, interstitial	—	—

5. Perivascular fat cells accompanying the blood vessels into the uterus.[20, 57, 60]
6. Inclusion of fat cells into the uterine wall during surgery.[56]
7. Fatty infiltration or degeneration of connective tissue in the uterus.[7, 28, 31]

Of these the most popular are (1) origin from misplaced embryonic cells and (2) the result of metaplasia of muscle or connective-tissue cells.

To discuss in detail each one of the theories is beyond the scope of this paper and no attempt is made to do so. In general, however, one is forced to wonder if the origin of the true lipomas is the same as of the mixed tumors. It is more likely that the pure lipomas arise from the misplaced lipoblasts or other lipomatous cell rests, and that the mixed types are the result of fatty degeneration or metaplasia of connective tissue and/or muscle, either from the uterine wall or from leiomyomatous tumors.

Pathology

Lipomas may occur anywhere in the uterus but are most frequently found in the corpus. In the combined series (true and mixed lipomas) only 12 per cent were present in the cervix. Some authors[47, 57] have postulated that the cornu was the site of predilection for these tumors, but in the literature only 9 lesions were specifically reported in that region and 6 others were described in the lateral walls. With these facts in view it is concluded that no portion of the corpus is favored. Of the ones present in the corpus 60 per cent were interstitial with the remaining 40 per cent about equally divided between submucous and subserous locations.

The size of the tumors varies from a few millimeters to 32 cm.[20] in diameter. Most of them, however, measure 5 to 10 cm. across. They are usually round but can be oval in shape, are sharply circumscribed, and look like leiomyomas on external examination. The consistency varies with the proportions of fat, muscle, and connective tissue. In general they are moderately firm. They are usually encapsulated and on cut surface show solid, dry or moist, yellow fat that bulges over the capsule. The larger tumors may be lobulated and may show areas of cystic or myxomatous degeneration.

Histologically, pure lipomas consist of adult fat cells lying in a scanty vascular connective-tissue stroma. Some authors, however, have described under the term of true lipomas tumors that in addition to the adult fat cells contain small amounts of muscle and connective-tissue cells.[15] They have regarded these as inclusions within the tumor mass.

Mixed lipomas vary greatly in their histological constituents. In some, adult fat tissue is so conspicuous, and fibromuscular tissue is so sparse, that their differentiation from true lipomas is difficult if not impossible.[70] In others

TABLE II. MIXED LIPOMAS

AUTHOR	AGE	LOCATION	SYMPTOMS	THEORY OF HISTOGENESIS
1. Lobstein	—	—	—	—
2. Seeger	53	Cervix	Bleeding	—
3. Lebert	—	Interstitial, corpus	—	—
4. Orth	—	Cervix	—	—
5. Brünings	55	Anterior, corpus	—	Metaplasia from muscle cells
6. von Franque	54	Cervix	Bleeding	Metaplasia from connective tissue
7. Knox	62	Interstitial, posterior corpus	Bleeding, pain, leukorrhea	Misplaced embryonal cells
8. Merkel II	63	Interstitial, posterior near right cornu	—	Misplaced embryonal cells along Wolffian duct course
9. Jacobsen and Chiari	67	Submucous, corpus	—	Metaplasia of muscle cells and fatty infiltration
10. Seydel	58	Interstitial, anterior near cornu (?)	—	Misplaced embryonal lipoblasts
11. Pollack	37	—	Bleeding	Traumatic inclusion of fat cells
12. Gebhard	56	Polypoid in the uterine cavity	Pain, bloody* leukorrhea	Metaplasia
13. Meyer lists 10 cases	40 — — — —	Interstitial 3 Subserous 3 Cervix Post. wall, pedunculated 2 Not stated	—*	Misplaced embryonal cells
14. Beneke and Walkhoff	81	Interstitial, anterior near right cornu	—*	Misplaced embryonal cells
15. Kelly and Cullen	62 50 29	Posterior, corpus	Bleeding Leukorrhea	Fatty degeneration of fibroids
16. Sitzenfry	62	Anterior, corpus	Abdominal distention,* foul leukorrhea	Misplaced lipoblasts
17. Englehard	63	—	Abdominal pain*	—
18. Kuttasow	60	—	—	—
19. Ley	54	—	—	Metaplasia of connective tissue
20. Smith	50	Subserous, pedunculated	—	—
21. Williamson and Brockman	66	Interstitial	—	—
22. Lockyer	51	Posterior wall of cervix	Bleeding	Metaplasia of muscle cells
23. Petersen	54	Submucous	—	Misplaced embryonal cells along Wolffian duct course

TABLE II—CONT'D

AUTHOR	AGE	LOCATION	SYMPTOMS	THEORY OF HISTOGENESIS
24. Lahm I	—	Cervix	—	—
II	—	—	—	—
25. Kruger	67	Submucous, right cornu	—	Misplaced embryonal cells
26. Askanazy	61	Interstitial	—	Misplaced embryonal cells
27. Starry	64	Posterior corpus, right side	Frequency and pressure	Lipocytic differentiation of a specific connective-tissue cell
28. Preissecker	51	Cervix	Bleeding, pain	1. Misplaced embryonal cells 2. Fat accompanying vessels
29. Dworzak	62	—	—	Misplaced embryonal cells
30. Plonskier	56	—	—	—
31. Springer	58	Anterior, submucous, corpus	Pain*	—
32. Bride	63	Posterior, corpus	Bleeding, abdominal enlargement	Fatty degeneration of fibroid
33. van Akkeren	63	Anterior, corpus	Bleeding, foul* discharge, pain	—
34. Glas	60	Cervix		
	64	Corpus		
	44	Corpus		
	63	Corpus		
	44	Corpus		Fat accompanying blood vessels
	38	Corpus		
	50	Corpus		
	56	Corpus		
	53	Corpus		
35. Baniecki	61	Corpus	Foul discharge, pain	—
36. Humphrey and Mustard	65	Corpus	Procidentia	—
37. Peake	45	Corpus	Bleeding, abdominal enlargement	Misplaced embryonal cells along Wolffian duct course
38. Kaseman I	58	Corpus, subserous, right	Bleeding, pain	Degeneration of fibroid
II	49	Corpus, posterior	Bleeding	
39. Hicks	57	Corpus, anterior	Bleeding, frequency	—
40. Riess	23	Subserous, near right cornu	Backache, pressure	Fat accompanying vessels
41. Dontenwill	57	Interstitial, anterior	Backache	—
42. Bruntsch	61	Posterior, left side	Bleeding	

*Show sarcomatous change.

there is such a marked predominance of muscle and connective tissue that they are difficult to distinguish from fibromas or leiomyomas.[27, 47] The majority of these, however, show a predominance of fat cells.

In either case the capsule usually consists of thin connective tissue. In some cases, however, there is not a marked delineation from the surrounding muscle and the tumor compresses the tissue with the formation of a pseudocapsule.

The most commonly associated pathological condition in the uterus is leiomyoma. In three cases there was an associated adenocarcinoma[9, 47, 64] and in one case an adenocanthoma[25] of the uterus. Chronic cervicitis is frequent. A liposarcomatous change has been described in seven cases.[2, 17, 19, 47, 65, 68, 74]

Clinical Manifestations

The clinical manifestations of these tumors are identical with those of leiomyomas. The patients may be completely asymptomatic. Of 41 patients with specific complaints, 51 per cent had some type of uterine bleeding. This bleeding varied from bloody leukorrhea or occasional spotting to menorrhagia, metrorrhagia, or persistent bleeding in the postmenopausal woman. Forty-nine per cent of the patients with symptoms had frank abdominal pain, heaviness, or pressure. Backache was also frequent. Other manifestations were abdominal distention and foul vaginal discharge in 8 per cent. The latter was most marked when the tumor had undergone a sarcomatous change.

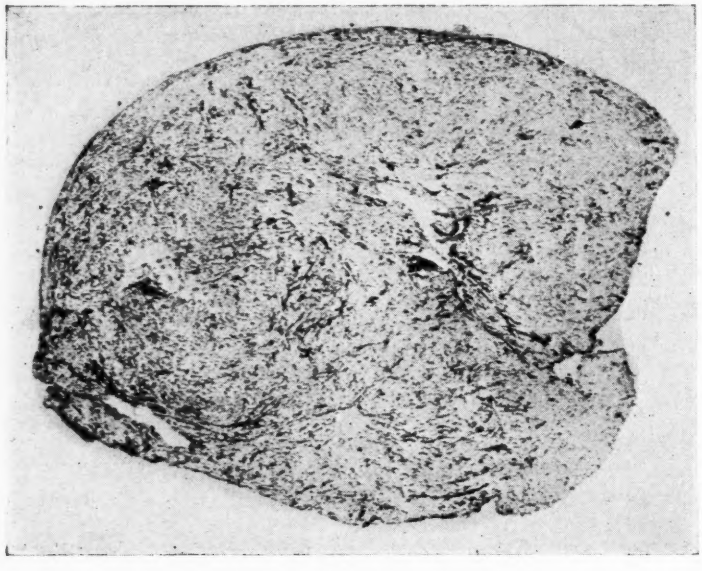

Fig. 1.—Entire lipoma showing thin capsule. (Hematoxylin and eosin. ×3.5.)

Diagnosis

The diagnosis of these tumors is only made at the time of operation or autopsy.

Prognosis

The prognosis in patients with pure or mixed lipomas, as expected, is good. For those with a sarcomatous change, it is guarded even in the absence of metastasis.

Case Report

M. B., a 72-year-old Negro woman, was admitted to the medical service of the Jefferson Medical College Hospital on July 5, 1952. She died three days later in coma. The clinical diagnosis was diabetes mellitus with Kimmelsteil-Wilson syndrome and uremia. Blood chemistry showed a blood sugar of 520 mg. per cent and blood urea nitrogen of 84 mg. per cent.

A postmortem examination disclosed: (1) benign nephrosclerosis, (2) intercapillary glomerulosclerosis, (3) bilateral bronchopneumonia, and (4) fibrinous pericarditis. As an incidental finding a lipoma of the uterus was found. The uterus measured 8 cm. from fundus to portio, 6 cm. transversely, and 4 cm. anteroposteriorly. The external os was narrowed to 1 mm. in diameter. The serosa was smooth and pink. In the left cornu there was a slightly elevated mass, 2 cm. in diameter. It was firm to palpation and on section appeared to be a leiomyoma.

Another small elevation was seen in the fundus posteriorly. On sectioning, it had the appearance of a lipoma. It measured 2 cm. in diameter and was located interstitially. The mass appeared well encapsulated and was easily "shelled out" from the myometrium (Fig. 1). The myometrium averaged 1 cm. in thickness. The endometrium measured 0.1 cm. in thickness.

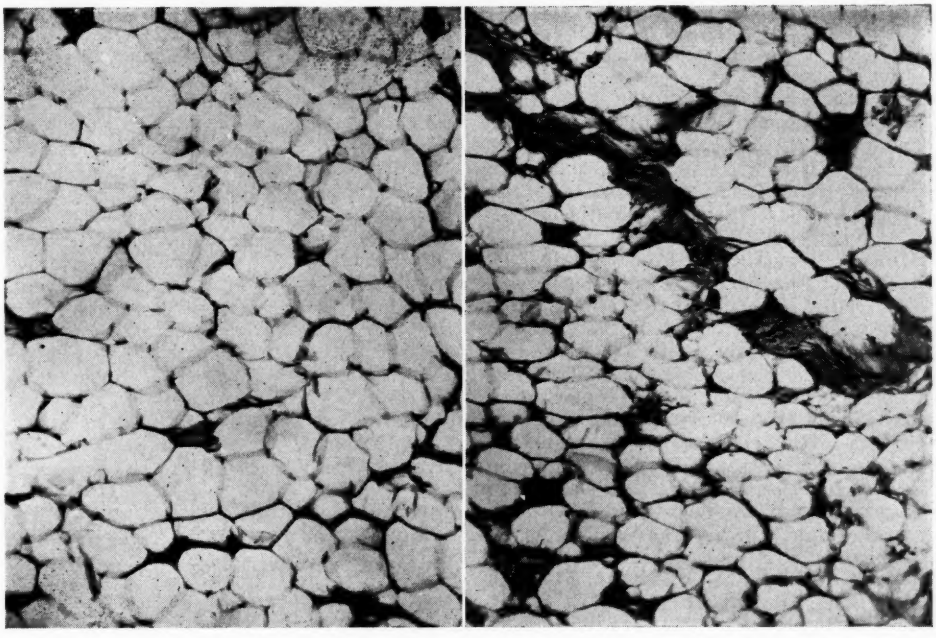

Fig. 2.—The tumor consists mainly of adult fat cells with inclusions of smooth muscle cells. (Hematoxylin and eosin. ×200; reduced ⅓.)

Histologically the endometrium showed senile changes, and there was a leiomyoma. The mass with the lipomatous appearance consisted of a well-defined tumor composed mainly of adult fat cells. Distributed through the scanty connective-tissue stroma, however, there were occasional strands of smooth muscle cells, particularly prominent in the periphery (Masson's stain) (Fig. 2). The capsule consisted of a mixture of muscle cells and fibrous connective tissue, the latter predominating. In the connective-tissue stroma there were a few thin-walled vessels. Our interpretation was that the tumor represented a true lipoma, with the muscle elements representing inclusions of normal myometrial cells as described in a similar case by Elkin and Haythorn.

Summary

1. Thirty-three pure uterine lipomas and 63 mixed lipomas have been recorded in the literature.

2. The tumors occur most frequently in postmenopausal women, particularly during the sixth and seventh decades.

3. The two most popular theories of histogenesis are (1) origin from misplaced embryonic fat cells and (2) metaplasia of muscle or connective-tissue cells.

4. The majority of the tumors occur in the corpus, interstitially, with the average size being between 5 cm. and 10 cm. in diameter.

5. Clinically, lipomas are indistinguishable from leiomyomas.

6. The diagnosis can be made only by laparotomy or at autopsy.

7. A true lipoma found in a 72-year-old woman is described.

Note.—We were unable to review the following case reports: Kuttasow, Pulsch, Birklein, Sivo, Chiari, and Kovats.

We wish to thank Dr. Karl A. Bolton for his extensive translation from the German literature and Drs. Peter A. Herbut, Lewis C. Scheffey, and Warren R. Lang for their constructive criticism.

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Addendum.—The following articles on the subject have been published since this paper was submitted for publication:

1. Degrazia, C. O.: Med. e cir. **25**: 115, 1953.
2. Robertson, J. W., and Gerber, H.: Am. J. Obst. & Gynec. **65**: 920, 1953.
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BENIGN CYSTIC TERATOMAS OF THE OVARY

A Clinico-statistical Study of 1,007 Cases With a Review of the Literature

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THE gross appearance of dermoid cysts of the ovary has given rise in the past to a host of fantasies and tales of witchcraft regarding their origin and behavior. Indeed, a century or two ago many believed these cysts were the price of unclean thoughts or spinsterhood. It remained for Pauly[58] in 1875 to refute effectively many of these misconceptions regarding the origin of these tumors.

That these fantasies existed is understandable since the totipotency of these tumors may give rise to many bizarre arrangements of tissue. Indeed, the appearance of sets of teeth inserted in firm bone, thick matted hair, or almost any other structure may be noted.

The term "dermoid" is the most popular because of the gross predominence of ectodermal elements. Actually, benign cystic teratoma is more accurate because these tumors are benign, cystic, and usually show derivatives from all three germ layers.

Benign cystic teratomas are believed to be associated with a high incidence of complications; it appears, however, that this concept is based on clinical impressions handed down to us and on statistics reported, mainly from Germany, around the turn of the century. Subsequent to that time, only a few series can be found in the literature which are large enough to be valuable, and unfortunately their incidences of complications are at variance or are not reported in detail. Certain individual complications, notably carcinomatous degeneration and intraperitoneal rupture, have received attention; however, the subject as a whole seems to need more adequate investigation and clarification. This study was undertaken with these thoughts in mind.

Material and Methods

This series of cases is based on records taken from the Armed Forces Institute of Pathology and the following hospitals in Baltimore: University Hospital, Saint Joseph's Hospital, Union Memorial Hospital, Lutheran Hospital, Mercy Hospital, Baltimore City Hospital, and South Baltimore General Hospital. No attempt was made to restrict this study to any time interval but rather to accumulate a large enough group of cases upon which to base valid conclusions. In all cases included in this study, the surgical specimen was submitted to pathological examination and when this was not available the case was discarded.

Incidences

Benign cystic teratomas are one of the most common of ovarian neoplasms, comprising from 5 to 25 per cent[7, 21, 27, 35, 73, 87] of all ovarian tumors (Table I). This rather wide divergence in reported incidences seems to be due, at least in part, to the inclusion of relatively small series. Quer[65] states that they comprise 10 per cent and MacCarty[40] 8.9 per cent of all ovarian cysts.

TABLE I. INCIDENCE OF BENIGN CYSTIC TERATOMAS AS NOTED IN VARIOUS REPORTS

AUTHOR	OVARIAN TUMORS	BENIGN CYSTIC TERATOMAS	PER CENT
Miller, J. W.	15,780	1,720	10.9
Olshausen	2,275	91	4.0
Geist	1,097	182	16.5
Linn	812	121	14.9
Kelly	555	90	16.2
Glass and Rosenthal	500	79	15.8
Smith, G. van S.	435	101	23.2
Meigs	327	60	18.3
Total	21,781	2,444	11.1

These tumors do not seem to have any definite predilection for one side or the other and in our series occurred on each side with about equal frequency. Although benign cystic teratomas are generally unilateral, they may not infrequently be bilateral, as may be seen in Table II.

TABLE II. INCIDENCE OF BILATERAL BENIGN CYSTIC TERATOMAS

AUTHOR	BENIGN CYSTIC TERATOMAS	BILATERAL	PER CENT
MacCarty	519	66	12.7
Marshall	415	63	15.0
Ottolenghi-Preti	256	35	13.7
Blackwell et al.	225	28	12.7
Geist	182	20	11.0
Linn	121	10	8.1
Batson	108	14	12.9
Smith, G. van S.	101	8	7.9
Total	1,927	244	12.6
Present series	1,007	112	11.1

Benign cystic teratomas may be found at any age, from 2 to 78 years in our series; however, they are most frequently found during the childbearing years. Pigne, cited by Pauly,[58] reported them to occur before birth and Pye-Smith[64] noted one in a 5-month-old infant. Costin and Kennedy,[12] reviewing 200 ovarian tumors in infants and children, found 25 per cent to be benign cystic teratomas. They reported 22 cases of their own in patients under 14 years of age, of which 7 were benign cystic teratomas. We noted 18 cases in patients under the age of 14, one of which occurred in a child 2 years old. It is of interest to note that 5 of the cysts in this age group had undergone torsion.

TABLE III. INCIDENCE OF DIFFERENT SIZES IN BENIGN CYSTIC TERATOMAS

BENIGN CYSTIC TERATOMAS	SIZE	PER CENT
127	0-5 cm.	12.6
608	5-10 cm.	60.5
198	10-15 cm.	19.6
38	15-20 cm.	3.7
36	20 or more cm.	3.6

In our series of cases, 923, or 91.6 per cent, occurred between the ages of 15 and 50, with the majority being found in the 20 to 30 year age group. This is somewhat at variance with the reports of others[21, 41] who noted a peak incidence in the 30 to 40 year age group.

The size of benign cystic teratomas varies considerably. In our group, the smallest was 2 cm. and the largest 45 cm. in size (Table III).

Symptomatology

A survey of the literature indicates that there are no pathognomonic symptoms associated with benign cystic teratomas. When these cysts do cause symptoms, they are those noted with any type of ovarian enlargement—notably pain, abdominal mass or swelling, and bleeding.

Pain is the most common complaint and is reported as a symptom in 27 to 96 per cent[7, 20, 21, 30, 73] of cases. We noted it in 480, or 47.6 per cent, of our patients. The distress may vary from a dull ache to the sharp, stabbing pain of torsion. More commonly, it is mild to moderate in degree and usually not related to anything in particular.

Abdominal mass or swelling is next in frequency and is reported to occur in 12.5 to 23.5 per cent[7, 18, 21, 30, 41] cases. In our series it was noted in 156, or 15.4 per cent.

There is widespread difference of opinion on whether benign nonfunctioning ovarian tumors can cause abnormal uterine bleeding. The proponents of this theory contend that it occurs on the basis of local pressure factors associated with displacement, pressure on, and congestion of, the uterus. Various authors[7, 18, 20, 21, 30, 41] report abnormal bleeding in 2.6 to 28.6 per cent of cases. We noted abnormal bleeding in 153, or 15.1 per cent, of our cases. It is not our purpose to enter into this difference of opinion; in the majority of our cases, however, the abnormal bleeding could more easily have been ascribed to other factors, such as fibroids, inflammatory disease, or functional bleeding. We did note, however, a small group of patients who reverted to normal cyclic bleeding after removal of the cyst, without any other therapy. The problem still remains to be answered.

Other symptoms noted, with lesser frequency, include bladder disturbances, gastrointestinal complaints, and backache.

Of almost greater interest was the unexpectedly high incidence of asymptomatic cysts found on routine physical examination, as part of a routine physical checkup or for other nonrelated disorders. A review of the reports by several authors can be found in Table IV.

TABLE IV. INCIDENCE OF ASYMPTOMATIC BENIGN CYSTIC TERATOMAS

AUTHOR	BENIGN CYSTIC TERATOMAS	ASYMPTOMATIC	PER CENT
Marshall	415	133	32.0
Ottolenghi-Preti	256	18	7.2
Blackwell et al.	225	57	25.3
Koucky	100	42	42.0
Silverman	82	5	6.0
Total	1,078	255	23.7
Present series	1,007	234	23.2

X-ray Diagnosis

One of the most useful adjuncts in the diagnosis of a benign cystic teratoma when an ovarian enlargement is discovered is thought to be x-ray. Yet, reading the reports of various authors, we find an extremely small percentage

of patients were x-rayed and a still smaller group had positive findings. One author[30] reported 10 patients who had x-rays and, although 8 had radiopaque bodies subsequently found at surgery, only 5 had pelvic shadows. Marshall[41] noted that in his large series none were diagnosed preoperatively although x-rays were extremely suggestive in 2 cases. Blackwell and his group,[7] analyzing 225 cases in 1948, reported that only 24 had been diagnosed and of these 12 were discovered or confirmed by the roentgenologist while reading films of the kidney, intestines, or pelvis.

Reviewing our series, we found that only 96 cases, or 9.5 per cent, were diagnosed correctly before operation and, of these, 62, or 64.5 per cent, were diagnosed or confirmed by x-ray. A total of 102 patients had x-rays, either in an attempt to make a correct diagnosis or, as was noted more frequently, in the process of a workup of the urinary or intestinal tract. In this group, 62 had positive findings suggestive of a benign cystic teratoma and the remainder were either reported as negative for radiopaque bodies or no mention was made of the ovarian mass.

It seems that we should resort more often to the use of x-ray and not be content with a simple diagnosis of ovarian cyst or, worse yet, adnexal mass. As McClellan[45] stated, "It is always a great gratification to the surgeon and worthy of his endeavor to have his operative findings agree with his preoperative judgment."

Radiopaque bodies have been reported to be found in 25 to 49 per cent[21, 41] of benign cystic teratomas examined after surgical removal. The incidence of correct preoperative diagnoses should, therefore, be at least this high. Care must, however, be exercised to remember that radiopaque shadows in the pelvis may also be due to ureteral calculi,[72, 80] phleboliths, calcified areas in a fibromyoma, lithopedion, and calcified lymph nodes.

Robins and White[68] have reported an additional aid in the diagnosis when radiopaque shadows are absent. They call attention to the presence of a rounded or ovoid mass, of decreased density due to the nature of the cyst contents, and encircled by a well-defined ring of increased density produced by the capsule of the cyst. The area of decreased density is banded or mottled, an appearance explained by hair mixed with sebaceous material.

Good[22] reviewed roentgenograms in 28 cases of benign cystic teratomas and found sufficient information to permit a positive diagnosis in 40 per cent.

Torsion

Torsion is the most common complication an ovarian tumor may undergo. Among 18 authors reviewed by Geist[20] its incidence varied from 2.4 to 76 per cent, although he noted its occurrence in only 7.4 per cent of his cases. It appears that its frequency has decreased since the beginning of the century, for at that time its incidence averaged around 20 per cent.[60, 70]

TABLE V. INCIDENCE OF TORSION IN BENIGN CYSTIC TERATOMAS

AUTHOR	BENIGN CYSTIC TERATOMAS	TORSION	PER CENT
Marshall	415	50	12.0
Ottolenghi-Preti	256	23	8.9
Sterer	248	43	17.2
Blackwell et al.	225	17	7.6
Geist	182	33	14.0
Batson	108	8	7.4
Koucky	100	3	3.0
Total	1,534	177	11.5
Present series	1,007	162	16.1

Many investigators agree that an ovarian cyst is more likely to undergo torsion than a solid tumor and the literature seems to substantiate this point. There is, however, no unanimity of opinion as to which type of cyst is most likely to become twisted, although most believe benign cystic teratomas undergo torsion as often as, or more often than, any other cyst. Wiener[87] noted that benign cystic teratomas constituted 30 per cent of 33 ovarian tumors with twisted pedicles and Sanes[69] found that these cysts comprised 33 per cent of twisted ovarian cysts.

The frequency of torsion of benign cystic teratomas has been surveyed in the literature, a summary of which may be seen in Table V.

Many theories have been offered to explain the occurrence of torsion. Intestinal peristalsis, alternate emptying and filling of the bladder, changes in size and position of the uterus during pregnancy and changes in the tumor itself are among those listed as internal factors. External factors that have been incriminated are those related to sudden changes in intraabdominal pressure such as are induced by vomiting or coughing, trauma, and laxity of the abdominal wall. Although these theories are interesting, agreement is lacking on any one, or group, as being important in the etiology of this condition. Opinion, however, is generally in accord with that of Frank[16] that medium-sized tumors are more likely to undergo torsion than either the small or large ones. Analyzing our series we found that of those cysts that became twisted, 89 per cent occurred in the group 5 to 15 cm. in size. This tends to support Frank's[16] opinion; we also found, however, that the benign cystic teratomas of this size made up 80 per cent of the entire series. Perhaps the medium-sized ovarian cysts merely appear to undergo torsion more frequently because they are the most common size found. It was of interest to find one case of a twisted benign cystic teratoma that weighed 15 pounds.

Torsion of a benign cystic teratoma causes embarrassment of its vascular supply, the degree usually depending upon the extent of twisting. A twist of 180 degrees will usually cause interference with both venous and arterial circulation, although we have noted several cases with up to as many as nine complete turns without any apparent obstruction of the blood supply.

When the degree of torsion is marked during an acute episode, gangrene commonly occurs and occasionally will lead to rupture of the cyst. One case was seen wherein this series of events occurred, resulting in intra-abdominal hemorrhage of over 1,500 c.c. of blood. Frank[16] reported a case of complete separation of the cyst, secondary to acute torsion with intra-abdominal hemorrhage.

If, however, the torsion does not cause sudden, complete loss of blood supply, collateral circulation may be established by adhesions to neighboring structures. Although further torsion is usually precluded by these adhesions, we noted one case of intestinal obstruction caused by torsion of the benign cystic teratoma and the adherent small intestine. Intestinal adhesions may also be the cause of eventual obstruction as was seen in a case with an adherent parasitic cyst which had migrated from the left adnexa to the right upper quadrant.

Hyalinization with calcification, or even bone formation, may occur when the blood supply is gradually lost. One such case was seen in our series, wherein a benign cystic teratoma, still attached to its attenuated, avascular pedicle, was completely calcified, even though it was 7 cm. in size.

Occasionally, the cyst may be completely detached from its pedicle to become parasitic. A few isolated reports[26, 32] are found in the literature of

this occurrence. It does not seem to occur as frequently as suggested by Koucky,[30] 2 of 3 cases of torsion, or Blackwell and his associates,[7] 2 of 17 cases of torsion, as we noted parasitic cysts in only 4 of our cases.

Infection is believed to occur more frequently when a benign cystic teratoma has become twisted; however, we failed to note torsion in any of our infected cysts.

There does not appear to be any definite evidence in the literature that torsion will occur more frequently on one side or the other. In our series, torsion involved each side with about equal frequency. Nine cases of unilateral torsion of bilateral benign cystic teratomas were observed; of perhaps greater interest, however, was the finding of three cases of bilateral, apparently simultaneous, torsion.

Infection

Benign cystic teratomas have long had a reputation for being susceptible to infection[16, 27] although no reason has appeared to explain this, other than theoretical grounds.[87] During the last century, these tumors were not infrequently infected, according to the literature of that time. The erroneous belief that these cysts are not only prone to infection but are quite commonly infected, has persisted to the present, in spite of several reports in the recent literature to the contrary (Table VI).

TABLE VI. INCIDENCE OF INFECTION IN BENIGN CYSTIC TERATOMAS

AUTHOR	BENIGN CYSTIC TERATOMAS	INFECTED	PER CENT
Marshall	415	17	4.0
Ottolenghi-Preti	256	10	3.9
Blackwell et al.	225	1	0.4
Batson	108	1	0.9
Koucky	100	3	3.0
Silverman	82	1	1.2
Glass	79	1	1.2
Spencer	59	2	3.4
Total	1,324	36	2.7
Present series	1,007	12	1.2

Numerous cases are found in the literature of infection of benign cystic teratomas by almost every type of organism, including typhoid, tubercle, and gas bacilli. Indeed, the older literature is notable for the variation of infecting organisms found in these tumors. Of interest were two reports[8, 55] wherein a benign cystic teratoma harbored typhoid organisms 16 years and 6 months, respectively, after the last clinical infection. More recently, the staphylococcus, streptococcus and colon bacillus are reported to be the main etiological agents, although occasional references are still found in the European literature to typhoid infection of a benign cystic teratoma.

Infection of the tumor may occur by hematogenous or lymphogenous routes and by direct extension from the intestines or as a result of an adjacent inflammatory process. It appears that pregnancy, torsion, and tapping are predisposing factors, for one or more of these conditions preceding the infection have been reported in many cases.

In our series, we failed to find any etiological or predisposing agent in 4 cases. In 3 patients with infected benign cystic teratomas, the cyst was noted to be densely adherent to the intestines and in two others suppuration occurred during pregnancy. The remaining cases were believed to be caused

by an appendiceal abscess, pelvic inflammatory disease, and colpotomy, respectively. Unfortunately, bacteriological studies were not carried out in any of our cases.

Infection of a benign cystic teratoma is thought to predispose the cyst to rupture, probably by increased intracystic pressure in conjunction with necrosis of the cyst wall. A review of our group of cases has led us to the same conclusion, for of 13 cases in which the cysts ruptured, 2, or 15.4 per cent, were infected. One of these was extremely interesting, for the infection occurred in a parasitic benign cystic teratoma and apparently caused it to rupture. At operation, this cyst was noted to be rather densely adherent to the intestines which no doubt contributed to the infection. This patient was discharged home feeling well after a somewhat stormy postoperative course.

Our experience has led us to believe that the treatment of choice in these cases is to cover the patient with a broad-spectrum antibiotic and then operate as soon as is feasible. Many of these patients fail to respond adequately to medical treatment, occasionally making it necessary to operate despite an elevated temperature. This was dramatically observed in one patient who failed to respond to medical therapy and ran a persistent temperature of 103 to 104° F. Her fever finally fell to 102° F. and she was operated upon immediately. The temperature returned to normal by crises and the postoperative course was smooth and uneventful.

Rupture

Although 2 per cent of all ovarian cysts are reported to rupture,[87] this is believed to be a rare occurrence in benign cystic teratomas, presumably due to the thickness of the cyst wall. Lippert,[35] however, noted rupture, both intraperitoneal and into a hollow organ, in 4.6 per cent of his cases. That rupture of all types of a benign cystic teratoma no longer occurs with this frequency is evident from Table VII.

TABLE VII. INCIDENCE OF RUPTURE IN BENIGN CYSTIC TERATOMAS

DATE	AUTHOR	BENIGN CYSTIC TERATOMAS	RUPTURE	PER CENT
1925	Koucky	100	2	2.0
1934	Meigs	60	2	3.3
1946	Blackwell et al.	225	2	0.9
1947	Poole	133	1	0.7
1951	Quer	400	4	1.0
1952	Silverman	82	1	1.2
1953	Batson	108	1	0.9
	Total	1,108	13	1.2
1954	Present series	1,007	13	1.3

The literature contains many single reports of this complication and in analyzing them it seems preferable to divide the subject into two main groups, intraperitoneal rupture and rupture into a hollow organ.

Kistner,[29] in his excellent review in 1952, was able to collect 20 cases of intraperitoneal rupture to which he added 2 of his own. Since his report, additional cases have been found,[5, 47, 73, 81] making a total of 27 cases of intraperitoneal rupture of a benign cystic teratoma reported to date. To this, we wish to add our 13 cases, all of which ruptured into the peritoneal cavity.

Unfortunately, no such extensive report has appeared on rupture occuring into a hollow viscus; therefore, no figures are available from the literature which would indicate its frequency. These cysts are thought to rupture into a hollow organ more frequently than into the peritoneal cavity.[29] Our experience has been to the contrary, for we failed to note a single case of rupture into

a hollow viscus. The literature contains many small series or case reports on rupture of a benign cystic teratoma into a hollow organ. These reports are generally found in the older literature which would also seem to indicate that rupture of this type does not occur frequently any longer.

Reviewing the literature, we noted that rupture has been reported into the intestines,[25, 54, 83] and the bladder[66] and even perforation of the abdominal wall.[61] Several instances of rupture into the rectum or sigmoid have been reported.[9, 10, 19, 37, 48, 86] The majority of these cases either accompanied or followed labor and in one instance[48] the cyst as a whole was expelled through the anus, the reporter being able to follow the pedicle up through the rent in the rectum. Bonney[10] also collected 6 cases in which benign cystic teratomas were driven through the vagina during labor and Koucky[30] reported one case of rupture into the vagina following labor. Other instances have been noted wherein rupture occurred into the Fallopian tube and the uterus.

Many explanations have been advanced to explain rupture of these tumors, among which torsion with infarction and gangrene, trauma, infection, and malignant degeneration are considered prominent. Many cases still remain unexplained, however, and other factors, such as prolonged pressure as would occur in labor, and "idiopathic causes"[65] must be considered important.

In our series, rupture occurred secondary to labor and delivery in 4 cases (31 per cent). One of these was a case of bilateral benign cystic teratomas, one of which, lying in the cul-de-sac, was ruptured. In 4 cases, the etiology must be considered idiopathic, as no demonstrable cause could be found. In 2 instances, the rupture was apparently secondary to infection of the cyst. The remainder of cases were equally divided among the following etiological factors: torsion, trauma, and tapping.

One would expect rupture of a benign cystic teratoma with intraperitoneal spill to produce signs and symptoms of an acute abdominal crisis. This, however, has not been our observation. Only 5 cases presented the picture of an acute condition on admission and only one of these had any degree of shock. In Kistner's[29] collected review, only 5 of 22 cases were reported as having an acute abdominal crisis. Why the irritating contents of these cysts fail to cause an acute episode of peritoneal irritation is difficult to understand, especially when at surgery one usually finds the major part of the peritoneal cavity involved by granulomatous adhesions.

Those patients who escape an initial intraperitoneal crisis usually consult a physician at some later date, often years later, complaining of progressive abdominal distention associated with gastrointestinal disturbances with anorexia, nausea, vomiting, or diarrhea present to some degree. The diagnosis is extremely difficult to make and often is not suspected until laparotomy for an abdominal mass. At surgery, the abdomen is generally found to be the site of a granulomatous type of peritonitis with multiple nodules, cysts, and adhesions. The peritoneal fluid may have an oily or fatty consistency. It is easy to confuse many of these cases with carcinomatosis or tubercular peritonitis and biopsy may have to be resorted to for an accurate diagnosis.

If rupture occurs into a hollow viscus, the situation is generally not suspected until hair, teeth, or sebaceous material is passed through the organ's natural orifice. At this time, the diagnosis becomes obvious. Heller[23] collected 25 cases from the literature in which passage of hair had occurred through the urethra.

The treatment of choice, once rupture of a benign cystic teratoma is diagnosed, is surgical intervention. Complete removal of the cyst is desirable. However, no attempt at removal of the neighboring granulomatous masses appears necessary. Reviewing our series, we find that in 2 cases complete

removal of the cyst was impossible and these patients were treated by partial excision and drainage. Both had prolonged postoperative courses but were discharged feeling well with the drainage sites closed. Unfortunately, no follow-up is available. In 3 other cases, the cyst was completely removed with drainage. Two patients had a normal postoperative course; however, the other died of pneumonia and persistent peritonitis, probably due to the fact that the cyst was infected. Three cases were treated by removal of the cyst without drainage and 5 others were handled by hysterectomy and bilateral salpingo-oophorectomy. All of these had an essentially normal postoperative course and were discharged feeling well.

If rupture occurs during surgical removal of a benign cystic teratoma, the treatment of choice appears to be copious lavage of the peritoneal cavity. Drainage does not seem necessary for in 12 cases closed without drainage in our series the postoperative course was uneventful. Four other cases were treated by drainage and the postoperative course was also normal.

Formerly, intraperitoneal rupture of a benign cystic teratoma was looked upon as being fatal in a great proportion of cases. Kistner's[29] collected review was the first to allow us optimism in the presence of this catastrophe. He noted that in 22 cases of intraperitoneal rupture, only 7 patients died during the postoperative period and all of these cases occurred prior to 1938. Our results are somewhat better, for we noted only one death in our series which, incidentally, occurred in the early 1930's. It is possible that this patient would have survived if the ruptured cyst had not been infected.

Pregnancy

Benign cystic teratomas have been reported to comprise 22-40 per cent[11, 44, 46, 78, 87] of ovarian neoplasms complicating pregnancy. The incidence of benign cystic teratomas complicating pregnancy can be seen in Table VIII.

TABLE VIII. INCIDENCE OF BENIGN CYSTIC TERATOMAS COMPLICATING PREGNANCY

AUTHOR	BENIGN CYSTIC TERATOMAS	PREGNANT	PER CENT
Quinland	52	2	4.0
Blackwell et al.	225	3	1.3
Glass	79	5	6.0
Furlong	79	1	0.8
Silverman	82	5	6.0
Batson	108	7	6.0
Total	625	23	3.7
Present series	1,007	129	12.8

Pregnancy is believed to increase the risk of complications to which ovarian neoplasms are ordinarily subjected, namely, torsion, rupture, infection, and malignant degeneration. Surveying our group of 129 patients suggests the same conclusion, for the incidence of complications was 24 per cent as compared with 19 per cent in the nonpregnant group. Although these figures are not statistically significant, one wonders what the incidence would have been if the 56 uncomplicated cases operated upon during the first two trimesters had been watched until term.

Torsion occurred in 25, or 19.3 per cent, and was the most common complication encountered. This figure is in accordance with Caverly's[11] 21 per cent, although somewhat lower than Spencer's[78] 33 per cent. All save 2 cases of torsion occurred during the prenatal period with the majority in the second trimester.

Infection was noted in 2 cases, one occurring during the third month and the other two weeks post partum. Both of these patients were treated surgically and had an uneventful postoperative course, the former going on to term and a normal vaginal delivery.

Rupture occurred in 4 cases. All of these were in the immediate postpartum period and were intraperitoneal in type. One was a case of bilateral benign cystic teratomas with the right cyst lying ruptured in the cul-de-sac after a difficult vaginal delivery. Many reports[29, 67, 78, 85, 87] are found in the literature of intraperitoneal rupture of a benign cystic teratoma during pregnancy, most of these occurring during or following vaginal delivery. Of a total of 40 cases of intraperitoneal rupture, 7, or 17.5 per cent, were noted during pregnancy or the puerperium. Two of these occurred during the seventh month and 5 in the immediate puerperium. As mentioned elsewhere, numerous reports have appeared of rupture of a benign cystic teratoma into the vagina, rectum, or sigmoid[10, 48] during or following labor. These are notable in the older literature; however, only one is found in recent reports[30] and none in our series.

One case of malignant degeneration of a benign cystic teratoma was discovered during pregnancy. To the best of our knowledge, this is the only case on record of malignancy in a benign cystic teratoma in association with pregnancy. The patient was operated upon during the fifth month of gravidity and the pregnancy continued on uneventfully to term. This case, along with the other malignancies in our series, will be described in greater detail as part of a future report.

As benign cystic teratomas have a tendency to remain within the confines of the true pelvis, 72 per cent in Caverly's[11] series, they are in an excellent position to obstruct labor. This complication, "tumor previa," was noted in 18 cases, or 14 per cent of our pregnant patients. Of those who went to term, 48 patients, or 37.5 per cent, had dystocia. Cesarean section, followed by removal of the obstructing cyst, was done in all but one of these cases. In the one remaining case, a difficult vaginal delivery was followed by surgery, because of rupture of the obstructing cyst as previously noted.

In 6 cases, the patient had what was described as a normal vaginal delivery, in spite of the known presence of the cyst, without any complications in the puerperium. Two of these cysts, however, were only 3 and 4 cm., respectively, in size when removed two months later. In 18 other patients, the presence of the benign cystic teratoma was not suspected until after vaginal delivery or the checkup at the sixth week. This indicates that not all of these cysts cause dystocia.

In spite of the fact that "tumor previa" is a complication peculiar to pregnancy, it should be included when one considers the over-all incidence of complications. We noted that 49 cases, or 38 per cent, of benign cystic teratomas associated with pregnancy were complicated. Caverly[11] noted 30 per cent in his series.

Bilateral benign cystic teratomas associated with pregnancy have received a great deal of attention in the modern literature. This interest was initiated by the report of Andrews and his associates[4] in which they collected a total of 43 cases from the literature and added a case of their own. Subsequently, several other reports have appeared,[1, 5, 6] bringing the number of bilateral benign cystic teratomas associated with pregnancy to 72. To this we wish to add 3 cases of our own.

Unfortunately, most of these reports have dealt with the surgical aspect of this problem and fail to mention the presence of complications. In 7 cases reviewed, including our 3, elective cesarean section was done for "tumor

previa." If we discount one of our cases, operated upon at three and one-half months, we note that 66 per cent of these bilateral cysts caused dystocia at term which warranted cesarean section. In one patient who was allowed to deliver vaginally, one of the cysts ruptured.

The patient who was operated upon at three and one-half months of pregnancy had both cysts resected, which also required the removal of the corpus luteum of pregnancy. Her postoperative course was uneventful and the pregnancy continued to term without hormone therapy. This conservative management is in accordance with that advocated by many authors.[14, 20, 24, 33, 50, 76]

When a benign cystic teratoma is discovered during the first trimester of pregnancy, it appears to be the wisest course to defer operative removal, in the absence of complications, until the fourth month of gravidity. At this time, the risk of abortion, even if the corpus luteum is removed, is greatly decreased. In our series of 82 patients operated on during the first or second trimester, only 2 patients aborted following operation. Information, unfortunately, is lacking in many cases as to whether hormone therapy was given postoperatively. Three other patients aborted prior to surgery.

If the cyst is found during the fourth or fifth month of gravidity, it is generally conceded that surgical intervention is indicated at the earliest opportunity. When the benign cystic teratoma is first discovered, during or after the sixth month of pregnancy, it appears preferable to delay operation, in the absence of complications, until term. At this time, examination will show whether the cyst is in a position to cause dystocia. If it is, cesarean section followed by removal of the cyst is indicated. Those patients whose tumor is lying in the abdominal cavity may be allowed to deliver vaginally. We wish, however, to emphasize the importance of surgical intervention as early in the puerperium as is possible. The wisdom of this is well documented by the older literature, wherein we find numerous reports of rupture, suppuration, or torsion occurring after delivery. It is further substantiated by finding that 22 per cent of our patients who did deliver vaginally subsequently developed torsion, rupture, or infection in the puerperium which required surgical intervention.

Malignancy

The reported incidence of malignant degeneration occurring in benign cystic teratomas is surprisingly low, as may be noted in Table IX.

TABLE IX. INCIDENCE OF MALIGNANCY IN BENIGN CYSTIC TERATOMAS

AUTHOR	BENIGN CYSTIC TERATOMAS	MALIGNANCY	PER CENT
Martzloff	200	2	1.0
Counseller and Wellbrook	408	7	1.7
Geist	183	2	1.0
Ottolenghi-Preti	256	1	0.4
Total	1,047	12	1.2
Present series	1,007	8	0.8

Although numerous reports are found in the literature of this complication, Masson and Ochsenhirt[43] in 1928 were able to collect only a total of 33 cases of squamous-cell carcinoma which they considered acceptable on the basis of gross and microscopic description and appropriate photomicrographs. To this, they added 3 cases of their own. Alznauer[2] in 1953 collected an additional 24 cases to which he added 3 of his own. Our survey has brought to light 7 more cases[7, 20, 59, 84] not included in their reports. To this total of 70 acceptable cases of squamous-cell carcinoma arising in benign cystic teratomas, we wish to add 6 cases of our own.

While practically all of the malignancies arising in benign cystic teratomas are squamous-cell carcinomas, other varieties have been described, namely, basal-cell carcinoma,[63, 77] sarcoma,[3, 36, 59, 71, 79] and adenocarcinoma.[51, 63, 74, 84, 88] We noted one basal-cell and one adenocarcinoma in our series. Not included in our group, however, are 3 cases of adenocarcinoma and one of sarcoma. In these patients either the disease was too extensive, or the operator's description too scanty, to enable us to be sure that the benign cystic teratoma was the primary site of the malignancy. Unfortunately, the literature has not been adequately surveyed and the total number of these less common types of malignancies is at present unknown. It is our intention to investigate the literature more thoroughly and to make this the basis of a future report.

It has been suggested by many investigators that we are doubtless missing many early cases of malignant degeneration of these cysts. That this may easily be true was suggested to us by finding in 2 cases that the malignancy was restricted to one tiny area of one slide with the remainder of the initial sections being negative for malignancy. Inasmuch as many malignancies arise in the "dermoid plug,"[20, 38] careful pathological examination of this area, in addition to any suspicious or unusual portions of the cyst, may uncover this complication more frequently.

There does not seem to be any particular predilection for one side or the other, as malignancies are seen occurring on each side with about equal frequency. Eisenstadter[15] stated that malignancy is more prone to occur when the cysts are bilateral; however, this has not been our experience, nor is it substantiated by the literature.

Unfortunately, there are no characteristic symptoms which would lead us to suspect malignant degeneration of a benign cystic teratoma until metastases have occurred. In our series, the diagnosis was not suspected until the surgical specimen was submitted to pathological examination in all but one case.

The prognosis in these cases is poor.[2] In Alznauer's[2] series of 32 patients known to have either died or lived for five or more years, there was an 87.5 per cent mortality rate at the end of five years. Geist[20] cited a series of 26 patients reported by Gorisontow, all of whom died. Lapouge[31] reported upon one patient who survived for seven years after operation, only to succumb to a recurrence of the malignancy.

In our series, two patients survived for five or more years and one is alive and free of the disease at the end of three years. One died of her malignancy in four months, another died of other causes in five months, one other died of diabetic gangrene of the leg in six months, and another, free of apparent malignancy, died in four years of advanced cardiovascular disease. Unfortunately, in 2 cases there is no available follow-up.

It has been stated in the literature[47] and noted by us that the prognosis seems to depend more on whether the cyst wall has been penetrated by the malignancy than on its pathological grading. This point will be more adequately discussed in our future report.

Treatment

The treatment of benign cystic teratomas is, without doubt, surgical removal. Although this concept is not new, we feel that certain aspects warrant emphasis.

In a review of the case histories of patients operated upon for a benign cystic teratoma, it was noted that several had a history of having a benign cystic teratoma removed at an earlier date. One doubts that all of these women could have been spared the second operative procedure. It is unquestionable, however, that many could have been, if adequate evaluation of

the opposite ovary had been performed at the time of the initial operation. In some cases, cysts up to 10 cm. in size were removed at the second operation which followed the first by only 1 or 2 years.

The frequency with which these tumors occur bilaterally, 11.1 per cent in our series, places a definite responsibility on the surgeon to inspect the opposite ovary carefully in all cases of an apparently unilateral cyst. If the ovary is enlarged to any degree, bisection may be necessary before one can definitely rule out a tiny benign cystic teratoma. In the few cases where this was done, one cyst was discovered.

We have previously emphasized the desirability of resection of the cyst in all cases of bilateral benign cystic teratomas. Resection should not, however, be restricted to just those patients with bilateral cysts, but is indicated in all cases wherein the tumor has not destroyed the remaining ovarian tissue. In these days of earlier diagnoses, better pre- and postoperative techniques, and improved anesthesia, we are able to detect and remove these cysts while many are still small. Advantage should be taken of this situation by preserving ovarian tissue whenever possible.

Summary and Conclusions

1. A detailed clinico-statistical study of 1,007 cases of benign teratoma of the ovary is reported and the literature reviewed.

2. Benign cystic teratomas have been reported to comprise an average of 11.1 per cent of all ovarian tumors, 12.6 per cent of which are bilateral. Our incidence of bilateral benign cystic teratomas was 11.1 per cent.

3. These cysts may be noted in both extremes of life; however, we found 91.6 per cent between the ages of 15 and 50, with the majority in the 20 to 30 year age group.

4. The symptomatology caused by these tumors is not pathognomonic and although pain was noted in 47.6 per cent, abdominal mass or swelling in 15.4 per cent, abnormal bleeding in 15.1 per cent, 23.2 per cent were asymptomatic.

5. Torsion occurred in 16.1 per cent of our series of benign cystic teratomas and was the most common complication encountered. Nine cases of unilateral and 3 cases of apparently simultaneous bilateral torsion of bilateral cyst were noted. Some of the sequelae to torsion were discussed.

6. Infection, although clinically believed to occur quite frequently, was noted in only 1.2 per cent of our series. Idiopathic causes, intestinal adhesions, and pregnancy were the important predisposing factors in our cases.

7. Although benign cystic teratomas are believed to rupture only in rare instances, we found the incidence of rupture to be 1.3 per cent. Twenty-seven cases of intraperitoneal rupture have been collected from the literature, to which we wish to add 13 cases of our own, making a total of 40 cases reported to date. Probable etiological factors and the management of this complication were discussed.

8. These cysts were associated with pregnancy in 12.8 per cent of our series. In the pregnant group, we noted that 38 per cent of these tumors became complicated. The complications and management of these cysts during pregnancy were briefly outlined. Seventy-two cases of bilateral benign

cystic teratomas have been collected from the literature, to which we wish to add 3 additional cases noted in our series. This brings the total to 75 cases reported to the present.

9. Our incidence of malignant degeneration of benign cystic teratomas was 0.8 per cent. Six cases of squamous-cell carcinoma, one basal-cell carcinoma, and one adenocarcinoma were noted in our series. Seventy cases of squamous-cell carcinoma have been collected from the literature, to which we wish to add our 6 cases, making a total of 76 cases reported to date.

10. Certain aspects of the surgical treatment of these cysts were briefly discussed.

We wish to extend our appreciation to the personnel of the medical records section in each of the hospitals used in this study, without whose efforts this report could never have been made. Special acknowledgment is due Mrs. Sutton in the University Hospital Medical Records section and Colonel R. M. Thompson, USAF(MC), Deputy Director of the Armed Forces Institute of Pathology.

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MANAGEMENT OF ANOMALIES OF THE GENITAL TRACT*

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THE cases of anomalies of the female genital tract admitted to Michael Reese Hospital during the past seventeen years have been studied for the purpose of evaluating their clinical significance, the reason for hospitalization, the diagnostic methods employed, and the management. In this series there were 35 patients who received some form of therapy for their anomalies, or were treated for pregnancy (Table I). In addition there were 9 patients in whom anomalies were found during the course of surgery for other reasons, or who were admitted to the hospital for some diagnostic procedure. This study does not include a consideration of pseudo- or true hermaphroditism or congenital vaginal cysts.

TABLE I. TYPES OF ANOMALIES ENCOUNTERED

Failure of fusion of cloaca and Müllerian tissue with complete development of uterus, tubes, ovaries	2
Absence of cervix and upper two-thirds of vagina	1
Absent uterus, tubes, upper two-thirds of vagina	1
Absent vagina, rudimentary tubes, and left uterus, absent right uterus, granulosa-cell tumor of left ovary	1
Bilateral rudimentary uterus and tubes, associated with endometriosis of appendix	1
Unicornate uterus	2
Double fimbriated end of tube	1
Absent right ovary, dermoid cyst of left ovary, tubes represented by fibrous cords	1
Right tube fibrous cord, right ovary represented by a small vesicle, torsion of left tube and ovary	1
Septate uterus	6
Uterus bicornis unicollis	7
Uterus bicornis bicollis	9
Rudimentary vagina, absent labia	1
Absent uterus, vagina, and proximal two-thirds of tubes	1
Total	35
Other anomalies brought to hospital for diagnostic study or found in the course of other surgical procedures	9

The importance of urological studies in anomalies of the generative tract cannot be emphasized too strongly.[2, 4, 5] Collins[6] reported an incidence of 89 per cent genital anomalies in the female patients in a group of 231 patients with renal agenesis. One of the rare anomalies that occurs is unilateral absence of the kidney, ureter, tube, ovary, uterus, broad and round ligaments. Less than 40 such cases have been reported at this time.[7] Danger of injury to a solitary pelvic kidney in a case associated with absence of the vagina during

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the attempt to create an artificial vagina has been stressed.[8] Everett[9] emphasized the dangers from a pelvic kidney in labor and cited two deaths which occurred post partum from renal failure resulting from compression during labor.

The various diagnostic methods for determining the type of anomalies of the generative tract have been adequately described in the literature, namely, use of the x-ray with Lipiodol instillation into the uterus, transvaginal and transabdominal pneumoperitoneum, and the use of uterine sounds or probes.

Monie and Sigmundson[10] proposed a classification for reporting congenital anomalies of the uterus and vagina and requested that, even if their classification were not used, details should always be given about the uterine body, cervix, and vagina, even though only one of those structures is abnormal.

In our series we have had no instances of uteri with a rudimentary horn. Tien[11] has reviewed the literature and reports a case of this anomaly. Another case report[12] was found of a simultaneous pregnancy in a rudimentary horn and in the normal horn, in which the rudimentary horn with its tube and ovary were removed, followed by delivery at term per vaginam from the remaining horn.

Failure of Fusion of Müllerian and Cloacal Tissues

We have treated 2 such cases. The first was previously reported.[13]

The patient was first seen at the age of 16 years, complaining of a mass in the lower abdomen, and of never having menstruated. Digital examination showed that the vagina ended in a pouch not more than 2 cm. deep. Rectoabdominal examination disclosed a mass about the size of a four months' gestation, similar in outline to a uterus. Pyelography showed a normal urinary system. Transabdominal pneumoperitoneum demonstrated that the approximate distance between the tiny vaginal vault and the lower pole of the uterine mass was approximately 6 cm. Surgical correction was accomplished by a transverse incision into the vaginal pouch; blunt and sharp dissection was made through the intervening tissue. The mass was brought closer to the vagina by abdominal pressure. The lower pole of the mass was grasped with a tenaculum and sutured to the vaginal pouch with mattress sutures. The cervical canal was identified and dilated. This was followed by the escape of 12 ounces of black menstrual blood.

On examination eighteen months later, the lower pole of the uterus was flush with the vaginal vault, but no vaginal cervix could be found despite the recurrence of menstruation at twenty-six-day intervals, lasting five days. Four years after surgery the patient married and became pregnant one month after discontinuing the use of contraceptives. Delivery was accomplished by elective laparotrachelotomy of a full-term, 7 pound 12 ounce male. A degenerated fibroid was excised from the region of the right round ligament. The choice of abdominal delivery was decided upon at term because there was neither a detectable cervix nor a detectable orifice in the vaginal vault. In 1950 this patient was again delivered by cesarean section. In 1953 the patient again became pregnant, and at three months began to have cramps and bleed. The products of gestation were not extruded, however. It was believed that the cervix had failed to dilate. Operative intervention showed that a diaphragm persisted, dividing the vagina into proximal and distal chambers. The conceptus was found lying in the proximal portion of the vagina. A normal 2 cm. dilated cervix occupied the vaginal vault. At a later date the diaphragm was removed surgically resulting in a vaginal canal of normal depth and capacity.[29] This patient, therefore, had an anomaly similar to that described by Henderson[30]—a congenital absence of the lower half of the vagina.

The second case was that of A. C., a 29-year-old unmarried white woman who had never menstruated, but for the past year had had lower abdominal cramps every twenty-eight days. Examination disclosed normal external genitals and secondary sex characteristics. Rectovaginal examination showed a short vagina ending in a blind pouch apparently separated from the cervix by a bridge of tissue 2 cm. thick. The uterus felt normal and bilateral cystic adnexal masses could be felt. In 1943 a vaginal plastic operation was performed with excision of the septum of connective tissue between the cervix and lower vagina. This patient subsequently married but never menstruated.

Incomplete Development of Müllerian Tissues

An example of incomplete development of the Müllerian tissues with lack of fusion with the cloaca was illustrated by the following case.

Mrs. C. K. was a 23-year-old white woman with a history of primary amenorrhea, and a nine-year history of lower abdominal cramps occurring at monthly intervals and lasting three days. Examination disclosed the presence of small breasts, normal external genitals, and a normal vagina ending in a blind pouch. Bimanual examination revealed a mass above the vagina the size of a normal uterus, and bilateral cystic adnexal masses. At laparotomy bilateral chocolate cysts of the ovaries, hematosalpinx, and a uterus without a cervix were found. A bilateral salpingo-oophorectomy and defundation of the uterus were performed. The pathologist reported fibrocystomas of the ovaries, fibrosis of the tubes with dilatation, Wolffian-duct structures in the walls of the tubes, and atrophy of the endometrial mucosa.

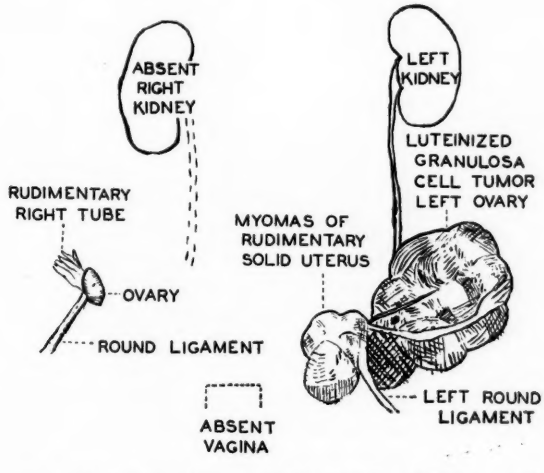

Fig. 1.—Mrs. M. Z. Congenital absence of right uterus, kidney. Rudimentary left uterus, granulosa-cell tumor of left ovary.

Absence of uterus, tubes, and the upper portion of the vagina was presented by Miss H. Z., a 23-year-old woman who complained of primary amenorrhea and pain in the lower abdomen recurring at monthly intervals. Transabdominal pneumoperitoneum revealed two markedly elongated and enlarged ovaries of the polycystic type; no uterus or tubes could be demonstrated. Operation consisted of plastic enlargement of the rudimentary vagina by a transverse incision into the vaginal vault and separation of the tissues between the bladder and the rectum.

Congenital absence of the vagina and uterus is illustrated by Miss A. D., a 24-year-old woman with the history of primary amenorrhea. Examination showed normal external genitals and absence of the vagina. Rectoabdominal examination revealed absence of the uterus. Transabdominal pneumoperitoneum showed two ovaries that were small, the distal portions

of the Fallopian tubes, and absence of the uterus. Operation consisted of the construction of a vagina by a transverse incision above the fossa navicularis and separation of the tissues between the bladder and the rectum up to the peritoneum. The mucosa of the labia was mobilized and sutured to the anterior and lateral walls of the space created, and a glass phallus was introduced.

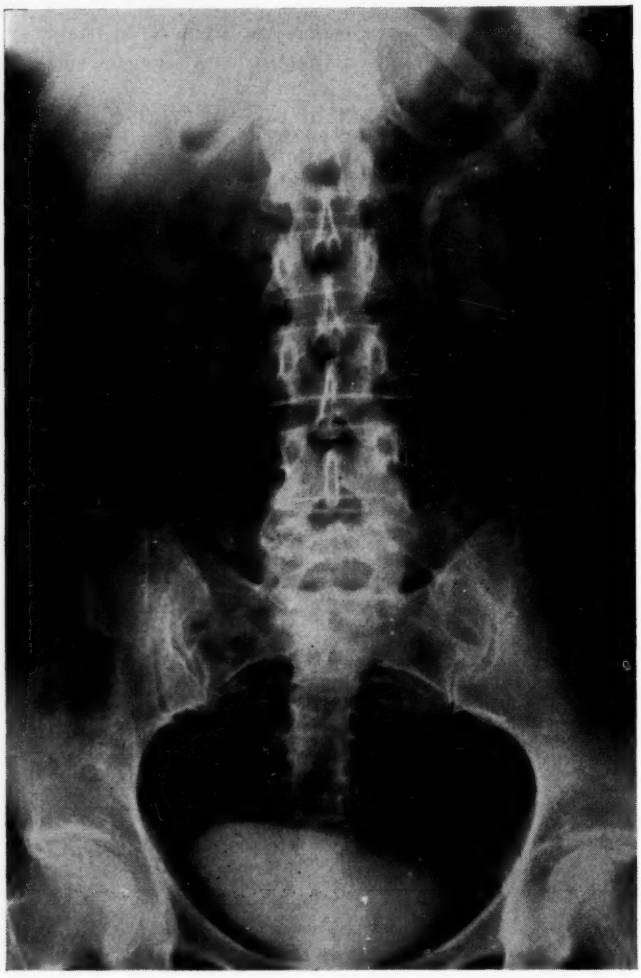

Fig. 2.—Mrs. M. Z. Excretory urograph taken one week after surgery revealed a normal-appearing left kidney, calices, and right ureter, but no excretory function was found on the right.

Absence of the vagina and cessation of development of the Müllerian system beyond the formation of the fimbriated ends of the Fallopian tubes, and an attempt at formation of a uterus on the left side is exemplified by the case of Mrs. M. Z., a 58-year-old woman. Her chief complaint was swelling of the abdomen of ten years' duration, associated with moderately severe low back pain. She had never menstruated. She had been married thirty-two years; her husband had died nine years before. Her mother had died of carcinoma of the stomach. Physical examination revealed a hard mass arising from the pelvis to a level of three fingerbreadths above the symphysis pubis. The vagina was absent but the vulva was normal. Rectoabdominal examination found no uterus, but a mass arising from the left adnexal region corresponding to the mass palpated on abdominal examination. Her blood pressure was 138/70; the hemoglobin was 63 per cent. On May 28, 1948, a

laparotomy was performed through a lower mid-abdominal incision. In the right iliac fossa was a normal-appearing small ovary with the fimbriated end of a tube attached to a round ligament which entered the right internal inguinal ring. In the left iliac fossa there were two golf-ball-sized fibroids attached to a round ligament which entered the left internal inguinal ring. There was a fimbriated end of a tube and a solid neoplasm 13 by 10 cm. in the region of the left ovary, which was adherent to the sigmoid colon. The ovaries, tubes, and myomas were removed. On exploration the right kidney and ureter were absent. The left kidney was in normal position and felt normal (Fig. 1). On cut section the left ovarian neoplasm was yellowish in color. Excretory urography taken one week after surgery revealed a normal-appearing left kidney, calices, and ureter, but no excretory function was found on the right (Fig. 2). The pathologist (Dr. Otto Saphir) reported luteinized granulosa-cell tumor of the left ovary, multiple myofibromas surrounded by circular smooth muscle, simple cysts of the right ovary, fibrosis of the rudimentary tubes, and parovarian cysts.

A case reported by McCall and Waugh[14] was similar in many respects to the one just described.

Their patient had an absent left kidney and ureter, incompletely rotated right kidney with normal function, and an incompletely developed vagina requiring construction of an artificial vagina and a plastic operation on the urethra. Operation revealed a fibroid tumor at the left pelvic brim, associated with a cystic left ovary, but absent left tube. On the right side the ovary was normal. There was a short right tube, no round ligament or uterine body. The left tube and fibroid were removed. No endometrial cavity could be found in the fibroid.

Another example of incomplete development of the Müllerian system associated with absence of the vagina is the case of Miss G. G., a 15-year-old girl.

Her chief complaint was primary amenorrhea and the occurrence of lower abdominal dull-to-sharp pain, intermittent, associated with nausea and vomiting and a low-grade fever on one occasion. These symptoms had recurred at monthly intervals for the past six months. Examination disclosed absence of the vagina and uterus. X-ray of the sella turcica showed no abnormalities. No evidence of broad ligaments, uterus, tubes, or left ovary was revealed by transabdominal pneumoperitoneum. Two spherical densities of approximately equal size were demonstrated adjacent to the right lateral pelvic wall. At laparotomy a normal-appearing ovary was at the left and the right pelvic brim. Rudimentary Fallopian tubes overlay the ovaries. A rudimentary uterus was present just below each ovary, to which a round ligament was attached. At the lower pole of each uterus was a fibrous cord which extended around the pelvic brim and joined just beneath the bladder. The right or larger uterus measured 3.3 by 4.4 cm. One surface was covered by a smooth membrane, on the medial surface there was hemorrhagic tissue from which blood was escaping. There was 200 c.c. of blood in the peritoneal cavity. The right uterus was removed. An appendectomy was also performed. The pathological report described a rudimentary uterus with a proliferating endometrium lining the cavity. No cervix could be demonstrated. The uterus was the site of acute and subacute metritis and parametritis. Acute catarrhal and acute superimposed on an organizing periappendicitis and endometriosis of the appendix were demonstrated. At some future time an operation for creation of an artificial vagina is contemplated.

Uterus Unicornis

Only two cases of unicornate uterus were present in our study. The first one was published in 1951 as a case report.[15]

The other is the case of E. S., a 43-year-old unmarried woman, who complained of profuse menses with the passage of clots for a period of three months. She also complained of bright red blood in the stools intermittently for the past six years. The past history was

otherwise of no importance. The family history was of interest because her mother died of carcinoma of the large bowel, her father died of carcinoma of the bowel, her brother died of carcinoma of the stomach, and her sister had had a retroperitoneal neurofibrosarcoma removed one year previously. X-ray studies of the bowel and proctoscopy showed no pathological condition to account for the bloody stools. Her blood pressure was 118/60. Examination showed an intact hymen. Rectoabdominal examination revealed a retroflexed uterus with a hard mass posteriorly measuring 6 cm. At laparotomy a unicornate uterus with a normal left tube attached and a normal left ovary were found. The uterus contained multiple myofibromas. On the right side was a rudimentary tube, a normal-appearing ovary, and a round ligament attached to the tube. No right kidney could be palpated. The operation consisted of a total hysterectomy and bilateral salpingo-oophorectomy. The pathologist reported multiple myofibromas of the uterus, with adenomyosis, proliferating endometrium, follicle and corpus luteum cysts of the ovaries. Postoperative excretory urography revealed that the right kidney was on the left side at the level of the third, fourth, and fifth lumbar vertebrae. The ureter of this kidney crossed over to the right side in the pelvis and showed no other abnormalities. The left kidney was rotated but otherwise normal (Fig. 3).

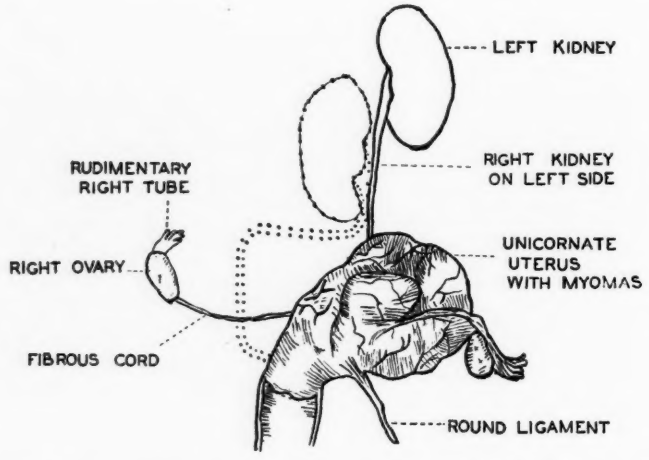

Fig. 3.—Miss E. S. Unicornate uterus, malposition of right kidney in left lumbar area.

Cases of Normal Fusion of Müllerian Tissues to Form a Normal Uterus but With Developmental Anomalies of Fallopian Tubes

CASE 1.—S. T., a 23-year-old gravida i, complained of vaginal bleeding and spotting for three weeks, associated with left lower quadrant pain of moderate intensity. She was first seen Dec. 2, 1948, and her last normal menstrual period was Nov. 8, 1948. On pelvic examination the left adnexa were tender. On motion of the cervix, pain was referred to the left lower quadrant of the abdomen and the cervix was cyanotic. A dilatation and curettage and posterior colpotomy were done, followed by a laparotomy. An unruptured left tubal pregnancy was found in the distal end of the left Fallopian tube which was the site of a double fimbriated end with two ostia. The right tube and ovary were normal. Subsequently this patient delivered a full-term baby on Dec. 19, 1950, and is pregnant again at this time (Fig. 4).

CASE 2.—R. K. was a 22-year-old unmarried gravida 0, whose chief complaints were severe dysmenorrhea, profuse menses, and left lower quadrant dull-to-sharp pain of four months' duration. Pelvic examination revealed hypoplasia genitalis and a left ovarian cyst 7 cm. in diameter. Laparotomy showed thin fibrous cords representing the Fallopian tubes. The right ovary was absent and a dermoid cyst was present in the left ovary. A resection

of the left ovary was done followed by a defundation of the uterus, in order to eliminate the menorrhagia. Since operation the patient has had monthly menstrual cycles, the flow lasting four to five days, a moderate amount of bleeding, and no dysmenorrhea.

CASE 3.—S. L., a 29-year-old married gravida i, para 0, entered the hospital on Dec. 15, 1949, complaining of sharp left lower quadrant pain of two days' duration associated with vaginal spotting. Her last menstrual period was Oct. 3, 1949. Pelvic examination showed a tender left adnexal mass 6 cm. in diameter. On the following day a dilatation and curettage were done revealing a large amount of endometrial tissue resembling decidual cast. At laparotomy, torsion of the left tube and an ovarian cyst with hemorrhage and infarction were found. The right ovary was represented by a 1 cm. blisterlike cyst. The distal two-thirds of the right tube was represented by a fibrous cord while the proximal one-third appeared normal and opened into the cornual end of the uterus. A left salpingo-oophorectomy was performed.

The pathologist's report was hemorrhage into a corpus luteum cyst, hemorrhage into the Fallopian tube with ghosts of villi. The endometrial scrapings disclosed a decidual cast.

Fig. 4.—Mrs. S. T. Ectopic pregnancy in Fallopian tube with double fimbriated end.

Anomalous Development of the Lower Genital Tract

Anomalous development of the lower genital tract occurred in a 28-year-old woman who was admitted to the hospital for surgical treatment of absence of the vagina. Her menarche occurred at age 13 with a four- to eight-week menstrual cycle lasting three to six days. On examination the patient had masculine distribution of pubic hair and no labia and no introitus were present. At surgery the patient was found to have a high perineum which obscured the urethral meatus. A 5 cm. perineotomy was performed, exposing the external urinary meatus at a level 3 cm. below the top of the incision, and the vaginal orifice was noted at this time. It readily admitted a No. 20.5 French dilator to a depth of 10 cm. The edge of the vaginal mucosa was then sutured to the skin of the perineum in a circular manner, thus creating two

labia minora. The patient became pregnant eight months later, had an uneventful pregnancy, and was delivered by laparotrachelotomy at thirty-eight weeks' gestation. In June, 1953, two years later, she had a missed abortion and the uterus was emptied by curettage.

Course and Management of Labor in Anomalous Uteri

There were 22 cases of anomalous uteri as shown in Table II. Six patients with uterus septus had a total of 23 pregnancies. There were 7 spontaneous abortions and 2 tubal pregnancies. The remaining pregnancies were full term and delivered vaginally except for elective cesarean section in 2 cases. In this small group of patients with septate uteri there was an increased incidence of abortion, tubal pregnancy, and breech presentation, but labor was normal, and vaginal delivery at term was the rule.

TABLE II. TWENTY-TWO CASES OF ANOMALOUS UTERI

	SEPTATE UTERUS	BICORNIS UNICOLLIS	BICORNIS BICOLLIS
Total number of cases	6	7	9
Total pregnancies	23	12	32
Abortions	7	0*	9
Premature deliveries	0	2	6
Vaginal deliveries at term	14	3	14
Cesarean sections	3†	6	3
Breech presentations	5	2	6
Tubal pregnancies	2	0	0

*Excision of pregnant horn of uterus.

†Two cesarean sections performed because of hysteroplasty on septate uterus. The third was done as a Porro operation for the purpose of sterilization.

In the group with uterus bicornis unicollis there were 7 patients who had a total of 12 pregnancies with no spontaneous abortions. The only abortion occurred at surgery when the pregnant horn was removed. Only 2 of these patients delivered vaginally. The remaining 5 patients were delivered by cesarean section for the following reasons:

CASE 1.—Mrs. M. P., a 33-year-old patient, had a cesarean section in her first pregnancy for antepartum hemorrhage at thirty-six weeks' gestation. A placenta previa totalis was found. An elective repeat section was done at the end of her second pregnancy, and the cornual end of the left tube was resected. The right tube and ovary were not visualized at this time and were considered absent because of the history of previous right adnexal surgery. Three months later a laparotomy was performed and the pregnant right horn was resected.

CASE 2.—Mrs. G. P., a 23-year-old gravida i, had a nine-hour test of labor at which time the cervix was 1 cm. dilated and the presenting part was at minus 3 station. The diagnosis of dystocia dystrophy syndrome was made and a low cervical cesarean section was done. A living baby weighing 4,250 grams was found in the right horn of a uterus bicornis unicollis.

CASE 3.—Mrs. H. Z., a 37-year-old gravida i, had an elective Porro cesarean section for multiple fibroids of the uterus, and schizophrenia.

CASE 4.—Mrs. S. T., a 25-year-old gravida i, had a right salpingo-oophorectomy for a papilliferous pseudomucinous cystadenoma, and endometrioma of the right ovary four years previously. The patient failed to go into labor at the time of her calculated due date despite the fact that the fetus seemed to be term sized. Three weeks later she had false labor for twenty-four hours. Four weeks after the expected date of delivery an elective low cervical cesarean section was performed. The baby weighed 2,515 grams. The pregnancy was in the left horn of the uterus.

CASE 5.—Mrs. M. L., a 27-year-old gravida i, had an appendectomy in the third month of this pregnancy because of right lower quadrant pain and tenderness. A pregnancy in the right horn of a uterus bicornis was found. She went to term and after a test af labor (duration not given), a low cervical cesarean section was performed.

Despite the high incidence of cesarean section in this group with uterus bicornis unicollis, one cannot conclude that cesarean section must be done so often because the indications were so variable.

In this group with uterus bicornis bicollis (didelphys) there were 9 patients who had a total of 32 pregnancies. There were 9 abortions, 6 premature labors, 17 full-term pregnancies, including 6 breech deliveries. In the entire group with uterus bicornis bicollis (didelphys) there were 3 cesarean sections done on 2 patients who were electively sectioned only because of the uterine anomaly. In 3 of these patients a vaginal septum was also present.

Only one patient in the group of uterus bicornis bicollis was unable to deliver a viable fetus.

Mrs. E. R., a 28-year-old gravida v, para 0, was Rh negative and her husband was Rh positive. She, however, did not develop any antibodies at the end of her fifth gestation which terminated at twenty-eight weeks. The fetus weighed 1,050 grams, and survived only two hours. Prior to this premature labor the previous gestations were spontaneous abortions, one of twenty weeks', and the remaining of eight weeks' duration.

In our cases of uterus didelphys there was an increased incidence of abortions, premature labors, and breech presentations.

The only death of a full-term infant in the neonatal period was in the case of Mrs. F. W., a 28-year-old gravida v, para iv, who spontaneously went into labor at thirty-six weeks' gestation. She had a four-hour first stage of labor. The presenting part was at plus 2 station in left occipitoposterior position. Much difficulty was encountered in attempting rotation of the fetal head. (Manual rotation was tried first, and then forceps rotation was tried unsuccessfully.) Further examination revealed a constriction ring present around the fetal neck. Deep ether anesthesia was given, and Adrenalin was administered intramuscularly, with resulting relaxation of the constriction ring and a midforceps delivery was accomplished without difficulty. The baby required resuscitation and survived only fourteen hours after delivery.

Hysteroplastic Operations on Septate Uterus

We had 2 cases in which the uterine septum was excised in patients who had had at least 2 abortions in gestations exceeding twelve weeks. In one the septum extended to the isthmus uteri; in the other it included the cervix.

Mrs. L. N., aged 28 years, had an appendectomy and right salpingo-oophorectomy in 1942 for an argentaffin tumor of the appendix, and papilliferous cystadenoma of the ovary. She had a spontaneous abortion at five months in 1945 and again in March, 1947. In August, 1947, transuterine pneumoperitoneum and Lipiodol instillation were performed, revealing a septate uterus. In September, 1947, at laparotomy a septate uterus was found. The uterus was incised in the midline from the fundus to the isthmus and the septum excised. The uterus was closed in layers. In March, 1949, the patient was electively sectioned at term after an uneventful pregnancy. She became pregnant again in 1951 and was delivered by cesarean section in February, 1952.

Mrs. B. I., a 27-year-old gravida iii, para 0, had 3 spontaneous abortions between three and four and one-half months' gestation, despite bed rest and hormone therapy. In 1947, Lipiodol instillations of the uterus through each of two cervices revealed two endometrial cavities well apart from each other. The films were interpreted to reveal a uterus bicornis bicollis. She had been having right lower quadrant pain for several years, but in May, 1951, the pain began to occur with greater severity and frequency, and was unrelieved by

diet, antispasmodics, or sedation. The patient also had progressive dysmenorrhea necessitating bed rest and was not relieved by administration of codeine. Examination was negative except for the pelvic findings of a vaginal septum occupying the proximal two-thirds of the vagina and separating the two cervices. In September, 1951, a laparotomy was performed, disclosing an arcuate uterus with a septum extending from the fundus to the cervices. The uterus was split open by an anterior midline incision, the septum excised, and the wall was closed with two layers of catgut. A small myofibroma was removed from the right anterior uterine wall. An appendectomy was also performed. It is too early to evaluate the results in this patient.

Monroe Kerr[16] described a case of uterus bicornis unicollis in which he performed a resection of the uterus producing a single uterine cavity followed by pregnancy and delivery at term per vaginam with difficulty because of a flat pelvis. The baby died forty-eight hours later. Subsequently, the patient became pregnant and was delivered at term of a normal baby by cesarean section.

The operation for removal of the uterine septum was first described in 1882 by Ruge and Schroeder. Subsequent operations for plastic unification of bicornate uteri were based on the works of the Strassmans,[17, 18] and more recently on the work of Jones and Jones.[19]

Comment

We wished to clarify the management of labor in the various types of anomalous uteri which were encountered and to determine which anomalies were most troublesome. Miller[20] feels that in reporting cases of labor involving anomalous uteri it would be wiser to designate each type of malformation, since each is characterized by different complications.

Way[21] presented a series of uterine anomalies which were mainly of the type that he called "uterus bicornis bicorporis unicollis." From his illustrations the type of uterine deformity described showed variance in the degree of fundal indentation from that of a uterus arcuatus, to that of a more deeply placed indentation corresponding to the type described in this paper as uterus bicornis unicollis. Several of his patients had a septum arising from the fundus from one-fourth inch to 2 inches in length. The 12 cases that he reported had a total of 33 pregnancies with the following complications: transverse lies, 12; abortion, 12; breech, 4; premature labor, 4; retained placenta, 3; prolapsed cord, 2; and placenta previa, 2. Four of these patients were delivered by cesarean section for the following: central placenta previa, transverse presentation with the umbilical cord presenting through a 1 cm. dilated os, transverse presentation with loss of the baby at previous delivery, severe pre-eclamptic toxemia of pregnancy at thirty-six weeks with the fetus in transverse presentation.

Findley[22] reported 3 cases of uterus didelphys and reviewed 132 other cases reported in the literature. In the 135 reported cases there were 17 full-term babies born with 6 fetal deaths, 13 breech presentations, 83 spontaneous abortions, and 15 premature deliveries. There were 23 cesarean sections, 2 Porro cesarean sections, one hemihysterectomy, and one craniotomy on a dead fetus. One maternal death resulted from rupture of the uterus. The indications for cesarean section were: delayed labor due to encroaching empty uterus, 5 cases; intrapartum convulsions, 2 cases; atresia of the vagina, one case; insufficient pains, one case; simple flat pelvis, one case; fear of thin uterine wall, one case; breech presentation, 3 cases. In the remaining 8 cases no explanation was given other than the presence of a double uterus. In one instance a double cesarean section was performed in a twin pregnancy.

Taylor[23] reported 9 cases of incomplete fusion of the Müllerian ducts. One was that of a patient with a uterus bicornis unicollis with a vestige of a vaginal septum who had two normal vaginal deliveries with toxemia of pregnancy in each gestation.

Falls[24] reported an incidence of 3.8 per cent arcuate uteri in 7,553 deliveries. The complications of labor were prolonged first stage of labor, an incidence of 10 per cent breech presentations, an increased incidence of transverse presentations, the occurrence of sudden intrauterine death of the fetus, retained placenta, and portpartum hemorrhage. In a series of 155 cases of arcuate uteri there were 21 cesarean sections, 4 destructive operations, 13 postpartum hemorrhages, and 3 manual removals of the placenta. The maternal mortality was 1.9 per cent. These patients died after prolonged tests of labor of forty-one, thirty-six, and fifty-two hours, respectively.

Schauffler[25] emphasized the importance of using uterine sounds in the nonpregnant state for the diagnosis of uterine anomalies, as well as using Lipiodol studies. He felt that repeated pelvic examinations during pregnancy to determine the changes in size and position of the nonpregnant horn were of prime importance in the management of labor in these patients.

We feel that more uterine anomalies might be found if uteri were explored after delivery in all cases of breech and transverse presentations, and immediately after an abortion in patients who have had repeated abortions.

Fenton and Singh[26] in their series of pregnancies associated with congenital anomalies of the reproductive tract reported an abortion rate that was three times that of the normal incidence. Only 56 per cent of their patients went to term. There was an increased percentage of breech and transverse presentations, intrapartum uterine inertia, operative deliveries, postpartum hemorrhage, and fetal mortality.

Baker and associates[27] recently reviewed the literature on pregnancy in 127 cases of anomalous uteri and reported 9 additional cases of their own. They analyzed the results of labor in each of the categories of anomalous uteri according to the classification of Jarcho. This type of information which is of great value to the student and practicing obstetrician has been lacking in the textbooks. There were 49 cases of uterus didelphys, and 59 cases of uterus bicornis unicollis vagina simplex. The incidence of abortion was highest in cases of uterus bicornis unicollis, 27 per cent. They feel as we do that cesarean section has no place in the management of pregnancy in a double uterus except in the presence of definite obstetrical indications.

Sheares[28] described a uterine anomaly named the helicoid uterus. He observed, in studying a large series of hysterosalpingograms and by examining patients under anesthesia, that the helicoid uterus was deviated to one side of the midline, one-half of the uterus appeared to be more anterior, and that this half of the uterus appeared to be better developed. In 8 of these cases a partial septum was found by sounding these uteri. He attributes this condition to an inequality in the rate of growth of the two Müllerian ducts. In a study of 48 infertile couples in which this anomaly was present the incidence of pregnancy was 11.8 per cent, which was one-third of the results obtained in the follow-up of a control group of cases.

Summary

1. A series of congenital anomalies of the genital tract have been presented, varying from absence of the uterus and vagina to almost complete fusion of the Müllerian ducts and partial development of the vagina.

2. Twenty-two cases of labor in septate and bicornate uteri were presented. We feel that conservative management of labor is the method of choice, and that cesarean section should be limited to those cases in which there is a definite obstetrical indication.

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Discussion

DR. JOHN W. HUFFMAN.—Dr. Lash has stressed the frequency with which anomalies of other organs occur concomitantly with genital malformations. Although none are present in his cases, congenital abnormalities of the lower intestinal tract are often associated with anomalous defects of the genital organs.

One of the problems is illustrated by the group of cases which were described as failures of fusion of the Müllerian and cloacal tissues. One patient had an apparent absence of the vagina with a uterus above it. The second patient presented a broad area of vaginal atresia. I think it is probable that these represent a failure of canalization of the vaginal plate rather than failure of the cloaca and Müllerian tissues. The management of cases of this type consists essentially of the construction of a copulative canal through plastic surgery and maintenance of that canal afterward by some type of obturator until coitus is possible.

The second group of anomalies are those in which the paramesonephric tissues fail to develop while the ovaries are present and functioning. In cases of this type the paramesonephric ducts on one or both sides fail to extend downward through the broad ligaments and genital cord. As a result, rudimentary uterine tubes and a rudimentary uterus may be present or these structures fail to form more than thin strands. The vagina is absent or is

represented by a dimple in the vestibule. Again, treatment is the establishment of a copulative canal and excision of any portion of the paramesonephric tissues which may be sufficiently developed to cause cyclic pain.

The 15-year-old girl who had bilateral rudimentary uteri interests me. I note that the operator removed the uterus from which blood was exuding and not the other. I wonder whether the remaining uterus might become functional and, perhaps, eventually cause symptoms.

The group of cases of anomalies of the Fallopian tubes leaves me in a quandary. Anomalies of the uterine tube, especially of the fimbriated end, are quite common. It is presumed that they may be a factor in tubal pregnancy, yet their etiological role has not been definitively determined. The development of the uterus should be affected if the upper portion of the paramesonephric duct, which creates the tube, does not form. Inasmuch as the paramesonephric duct, which is the progenitor of the uterine tubes and the uterus, grows downward, it would be anticipated that agenesis or marked hypoplasia of the tube would be associated with a very imperfectly developed uterus.

The case in which a very high perineum obscured the urethral meatus sounds as though it might be a failure of canalization or a problem similar to those seen in individuals suffering from prenatal adrenocortical hyperplasia. It would be of interest to know something of the state of the patient's clitoris, of her other genitals, and whether a 17-ketosteroid determination had been made.

The essayists pertinently pointed out the incidence of abortion associated with pregnancies in anomalous uteri. That an increased hazard accompanies gestation in a malformed reproductive tract is shown by the greater frequency not only of abortion, but of other complications of pregnancy and parturition which occur in such cases. The pregnant patient who presents a congenital anomaly of genitals deserves extreme vigilance on the part of the attending obstetrician.

Finally, discovery of congenital abnormalities of the genitals through examination of the newborn infant deserves emphasis. Their correction or identification during the postnatal period may overcome some of the difficulties which such individuals often face in later life.

DR. FREDERICK H. FALLS.—In Dr. Lash's presentation of material we got the impression that these uteri were uncommon over a period of years at Michael Reese Hospital and that only this small number of cases was seen. I am perfectly sure that at least five times that many cases occurred, and that this report represents only the ones that were recognized and not the ones that were present. It is very easy to overlook this anomaly. At the Chicago Lying-in Hospital in 1920 we had an old Italian woman, a para xiv, whom I saw in the outpatient clinic. She delivered the first baby normally, and after delivery she had appendicitis and apparently thereafter she never had a normal delivery. I assumed that adhesions developed and that these produced tranverse presentations and breech presentations in the various pregnancies. Nobody had made a diagnosis. In the fourteenth pregnancy cesarean section was performed and a bicornate uterus was found.

We have been observing this condition ever since 1920, when I had a case in which after two or three hours of labor suddenly the baby's heart tones stopped. I asked Dr. DeLee to listen to see if the baby was dead. He said the baby was dead but he did not know why. I inserted a bag into the uterus. After a desultory labor of twelve hours, I put my hand in the uterus to do a version and to see why the head was not engaging, and for the first time I knew the patient had a bicornate uterus. I did a version and delivered her, and two years later Dr. Greenhill wrote me that he had just delivered her and found a bicornate uterus septus and the hole in the septum which I made.

It is perfectly obvious that you cannot go into an active service for one month without seeing some type of bicornate uterus. As Dr. Lash has pointed out, the interesting thing is that most of these patients deliver normally and that therefore we have to be conservative in their management. It is also true that a large percentage of them will have minor complications which are not ascribed to the actual anomaly but are rather diagnosed

as complications possibly produced by the anomaly. We find in the very early months a difference in growth of the uterus. One side of the uterus grows more rapidly than the other. The side that is growing more slowly is firmer. In most of the cases the nonpregnant side is mistaken for a fibroid. As time goes on it rounds out and you no longer find the fibroid. As time goes on, particularly in the primipara, if you see an oblique position of the baby with the head in between the right iliac fossae and the breech under the spleen, you have to explain why that baby is not up and down horizontally. The explanation is the type of uterus. As the pregnancy advances you notice peculiar heart tones which will be rapid and slow. That irregularity is highly significant and characteristic of this particular condition.

In these cases I would say in the first place we should be sensitive to the fact that they are common, sensitive also to the fact that these uteri behave abnormally in pregnancy because we have an abnormal endometrium to start with. We note changes in the heart tones, malposition, and failure of completion of the third stage which results in hemorrhage, retained placenta, and other anomalies. Possibly inversion of the uterus occurs.

DR. A. F. LASH.—These anomalies fall into the following classification. First, among the children sent to me by pediatricians with so-called genital anomalies, I have found agglutination of the labia minora commonly. I think we can put the parents at ease by telling them that no plastic surgery is necessary. When we reach the teen-age group we meet the major deformities and there is not much we can do if there is a complete absence of the vagina except make the diagnosis. In the second decade, however, amenorrhea or sterility problems present themselves together with normal external genitals. I usually find it not advisable to create a vagina unless the patient is going to be married. Also in this group in the twenties, we have observed patients with typical ovarian agenesis. Then hormonal studies must be made as well as other studies. You will find the estrogen level is only 2 or 3 mm. instead of 8 or 10 mm., while the gonadotropins are high, 200 mg. instead of 40 or 50 mg. In spite of these studies all these patients must have exploration by laparotomy. In the third or fourth decade we see them as genital or pelvic problems, with either tumors or bleeding. I have had uterine and ovarian tumors associated with anomalies as described in the paper. I had a woman in the forties with carcinoma of the endometrium on one side of a uterus didelphys.

The importance of recognizing the anomalies during the childbearing period is illustrated by an instance of bleeding occurring from the nonpregnant side of a pregnant bicornate uterus. These patients require very careful study or unwarranted interference may be carried out, as bag induction on the normal pregnant side while the bleeding was occurring from the adjacent corpus.

DR. SIDNEY R. LASH (Closing).—To answer the question about the little girl with the two rudimentary uteri. She was just operated upon four months ago by one of the Staff so there is no follow-up.

To answer the question about the patient with the high perineum, and absence of external genitals, labia, etc. She did not have a large clitoris. She subsequently delivered a baby and following that had one miscarriage.

URETHRAL TRICHOMONIASIS IN THE FEMALE

A Possible Common Denominator in Recurrent Trichomonas Vaginalis Vaginitis and Recurrent Bacterial Cystitis

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TRICHOMONAS vaginalis infections of the vagina and bacterial cystitis usually due to *Escherichia coli* are two common diseases of adult women. The pathogenesis of each infection is obscure, the causes of recurrences are not well understood, and treatment is often unsatisfactory. Although the possibility that the two diseases may be related has not escaped notice, no explanation for an association between the two has been widely accepted. Dual infections when present have usually been considered to be coincidental because of the frequency of each disease; the therapy of the two diseases has also been discussed separately.

The purpose of this report is to present evidence that *T. vaginalis* is a common parasite of the female urethra as well as of the vagina and that this localization of the parasite in the urethra may be responsible for both the recurrences of *T. vaginalis* infections of the vagina and the development of bacterial cystitis. A similar relationship has been previously suggested by others.[1, 2, 3]

The Method

A series of women, examined routinely for vaginal trichomoniasis, were also studied for the incidence of urethral trichomoniasis. The patients were derived from three sources: (1) pregnant women being seen for the first time in the Obstetrical Clinic of The New York Hospital (17 cases); (2) patients with gynecological disorders being examined at the Strang Clinic (12 cases); and (3) private patients (15 cases). The studies were made by three different observers using a similar technique.

Vaginal exudate was obtained from the speculum used to visualize the cervix. The speculum was introduced without the use of a lubricant. Three wet smears were prepared by diluting the vaginal secretion with saline and then examined under the low and high power of the microscope for at least 10 minutes.

Urethral material was obtained by the following procedure. The urethra was firmly "stripped" by introducing a finger into the vagina and applying pressure anteriorly as the finger was removed; additional pressure was usually applied to the distal portion of the urethra in order to express the contents of Skene's glands. The urethral orifice was then opened and a pipette introduced for a distance of 1.0 to 1.5 cm., care being taken not to touch the meatus of the urethra. The drop of whitish material obtained in this fashion was expressed into a drop of saline, and the mixture was then examined microscopically.

The numbers of parasites were graded roughly from 0 (zero) to ++++ (four plus). If one to five parasites were found in the three smears the grade was + (one plus); 5 to 20 the grade was ++ (two plus), 20 to "many," the grade was +++ (three plus), and when several parasites were seen under the high-power magnification of the microscope the grade was listed as ++++ (four plus).

Results

These are recorded in Table I and summarized in Table II. Typical case reports illustrating salient points are reported in detail.

TABLE I. FORTY-FIVE CONSECUTIVE CASES OF TRICHOMONIASIS IN WHICH PARASITES WERE FOUND IN THE VAGINA, OR IN THE URETHRA, OR IN BOTH

	POSITIVE IN VAGINA	POSITIVE IN URETHRA		POSITIVE IN VAGINA	POSITIVE IN URETHRA
1	+++	+	24	++	+
2	++++	++	25	+	+++
3	++++	+	26	+++	+
4	++	+	27	+	0
5	++++	+	28	0	+
6	++++	++	29	++	++
7	++	+	30	0	+++
8	++++	+	31	+	+++
9	0	++	32	+++	+
10	+	+	33	0	++
11	+++	+	34	++	++
12	+++	++	35	++	++
13	+	0	36	0	+++
14	0	+	37	+	+
15	++++	++	38	+	+
16	++++	++++	39	++++	+
17	++++	+	40	++++	++
18	++++	++++	41	0	++++
19	++++	+	42	+++	++
20	+	++++	43	++	+
21	+	0	44	++	0
22	+	0	45	+++	+++
23	+	++			

TABLE II. SUMMARY OF TABLE I

Patients positive for *T. vaginalis*	45
Positive in vagina	38
Positive in urethra	40
Positive both in urethra and vagina	33
Positive in vagina and negative in urethra	5
Positive in urethra and negative in vagina	7

Case Reports

CASE 1.—(C. B.) The patient was a 23-year-old nullipara, gravida iii, who had three spontaneous abortions, each during the first trimester of pregnancy. Following the third abortion a serious effort was undertaken under expert gynecologic guidance to eradicate the severe vaginal trichomoniasis which had complicated each pregnancy. After two months of intensive therapy the trichomoniasis was considered cured. On a day in which no trichomonads were demonstrated in the vagina, Skene's glands were gently massaged and the entire length of the urethra "stripped"; a drop of whitish fluid was expressed. Examination of this drop under the microscope showed a large number of *T. vaginalis*, leukocytes, mononuclear cells, and epithelial cells. Culture of this material was positive for *E. coli*. This patient had had two attacks of cystitis due to *E. coli* during the preceding three years. At the time of this study she had no urinary symptoms and no vaginal discharge.

CASE 2.—(S. C.) The patient was a 20-year-old woman who one month following sexual intercourse for the first time became aware of intense leukorrhea with pruritus vulvae. Examination showed typical *T. vaginalis* infection with edema of the mucosa, and a heavy vaginal discharge containing myriads of trichomonads. After two weeks of treatment no parasites could be demonstrated in the vagina, but Skene's glands contained fluid with 8 to 12 organisms per high-power field. Despite treatment, recurrences of the vaginal infection were frequent. There was no history of cystitis.

CASE 3.—(B. F.) The patient was a 39-year-old woman who had developed *Trichomonas vaginalis* vaginitis 13 years before. Numerous efforts, involving the use of many drugs and different regimens, failed to prevent recurrences. She reasonably became impatient with the available modes of therapy and learned to "live with" and control her infection by douching with lactic acid solution or vinegar whenever symptoms returned.

Beginning 10 years ago the patient had a series of frequent attacks of typical cystitis with frequency, burning on urination, and pyuria. Cultures were invariably positive for *Escherichia coli.* In recent years treatment with chlortetracycline (Aureomycin) was rapidly effective in alleviating symptoms.

Originally the incidence of attacks was without obvious pattern but three years before the patient volunteered her belief that the attacks followed sexual intercourse, usually after a three-day interval. Examination of the partner could not be conducted but he was a healthy male who denied urinary disease. Chlortetracycline prophylaxis (administered orally, 1.0 Gm. daily for 3 days) between the time of intercourse and the expected date of cystitis was successful in preventing the development of a bladder infection.

Examination of the patient disclosed a few trichomonads in the vaginal secretion although no signs of vaginitis were present. A drop of exudate expressed from Skene's glands contained huge numbers of trichomonads. Cultures of this exudate were positive for *Escherichia coli.*

It appears likely in retrospect that trichomonads carrying *E. coli* entered the bladder during intercourse and produced a recurrent cystitis.

CASE 4.—(The case history will be reported in detail elsewhere.) The patient was a 41-year-old woman who has had vaginal trichomoniasis since her return from South America in 1946. Since 1951 her chief complaint has been recurrent cystitis. *Trichomonas vaginalis* has always been demonstrated in the urine at times of recurrence of the cystitis but usually in scant numbers. Irrigation of the bladder usually relieved her symptoms. When she was seen at The New York Hospital in November, 1953, a careful examination was made with the following results:

Exudate removed from posterior fornix: negative for *T. vaginalis* on hanging drop and culture.
Exudate removed from anterior fornix: negative for *T. vaginalis* on hanging drop and culture.
Exudate removed from cervix: negative for *T. vaginalis* on hanging drop and culture.
Exudate removed from vaginal introitus: negative for *T. vaginalis* on hanging drop and culture.

Urine: positive for *T. vaginalis* on hanging drop (one plus) and culture.
Urethral introitus: positive for *T. vaginalis* on smear (2 plus) and culture.
Exudate from Skene's glands: positive for *T. vaginalis* in smears (4 plus) and culture.

This examination was repeated in one week with the same findings.

One week after the second examination the patient was admitted to another hospital for extirpation of Skene's glands. The surgeon again repeated the tests before operating, with similar results.

CASE 5.—(R. K.) The patient was a 33-year-old woman who had her annual physical examination on Nov. 10, 1953. At that time the vagina and cervix appeared normal. Smears of the vaginal secretion and cervical scrapings prepared by the Papanicolaou method were negative for tumor cells. Review of the slides showed no trichomonads.

On Dec. 28, 1953, the patient developed symptoms of cystitis with frequency and a sensation of burning on urination. The urine contained many leukocytes, some in clumps, a few erythrocytes, a rare *T. vaginalis,* and two plus albumin. Culture was positive for *Escherichia coli* and several other organisms. The vaginal mucosa at this time was coated with a discharge containing many motile trophozoites of *T. vaginalis.*

The patient admitted that she had several sexual exposures during the last two weeks of November and the first two weeks of December with a new partner. Examination of this partner was not feasible, but it was known that his wife had had a *T. vaginalis* infection for over a decade.

The evidence in this case suggests that the patient acquired a *T. vaginalis* infection from a male who transmitted it from his wife. The cystitis associated with the presence of *Escherichia coli* could have been produced by the parasites carrying the organisms to the bladder. Weaknesses in this epidemiologic chain are obvious.

Comment

The data presented in Table I indicate a frequent association between the presence of *T. vaginalis* in the vagina and in the urethra. If repeated examinations had been done and if a culture technique had been employed, some of the negatives in Table I might have been found to be positives.[4]

Although 20 to 30 per cent of adult women harbor *T. vaginalis,* the epidemiology of the infection is poorly understood. Direct contamination, towels, toilet seats, swimming pools, etc., have from time to time been incriminated in the spread of the disease.[5] In recent years there has been increased interest in a venereal mode of transmission.[6] That trichomoniasis may involve the urethra of the male has been reported in several studies.[7, 8, 9]

Regardless of how the disease is acquired, there is general agreement that its cure is difficult. Several scores of medications in the forms of douches, inserts, powders, jellies, and insufflations have been employed for decades without great success. The parasite is extremely sensitive to noxious agents and many hundred preparations have been found which produce temporary disappearance of the parasite and alleviation of symptoms if they are present.[10] Often, however, the parasite returns or becomes associated with a recrudescence of the disease but it is not established whether this represents a "relapse" or a reinfection.

The data herein suggest that *T. vaginalis* may survive in the urethra, possibly in the paraurethral glands (Skene's), in mucosal crypts, or in the folds of transitional epithelium.[11] The possibility must be considered that *T. vaginalis* is in some cases a parasite of the urethra and that it only secondarily affects the vagina. In fact, *T. vaginalis* may be a "better parasite" of the urethra than of the vagina. An "ideal" parasite is one which survives in a host causing a minimum of damage. In the urethra the parasite apparently causes considerably less damage than in the vagina although adequate histologic studies are not yet available.[12] If this concept is correct, treatment limited to the vagina will often fail since the trichomonads may survive in the urethra and contaminate the vagina following urination or sexual intercourse.

Urinary tract infections are exceedingly common and cystitis in the female is one of the most frequent of these infections. Although many have indicated

the necessity of regarding cystitis as part of a more extensive disease such as pyelonephritis or "pyelitis,"[13] these infections from a clinical standpoint often appear to be localized in the bladder. The tendency to recurrence is well established.

Many difficult organisms have been incriminated as the cause of cystitis but almost all authorities agree that *Escherichia coli* is most often obtained in pure culture and that mixed infections (one organism usually being *E. coli*) occur in over half the cases.[14, 15, 16]

Explanations of the pathogenesis of cystitis are not entirely satisfactory. To explain the pathogenesis of recurrent cystitis in the female, the concept is proposed that bacteria reach the bladder on "the back" of *Trichomonas vaginalis.* From a practical standpoint the protozoan *Trichomonas vaginalis* is rarely separable from *Escherichia coli* or other organisms, especially staphylococci and streptococci. One may say dogmatically that except under laboratory circumstances every trichomonad carries bacteria with it. Trussell[17] has described how he worked for four years to obtain a pure culture of *T. vaginalis;* only the use of antibiotics today permits selective destruction of bacteria with preservation of the parasite.

Since *Trichomonas vaginalis* is a motile flagellate and since it has been demonstrated in the bladder and urethra, the possibility exists that it carries its bacteria to the bladder. In this manner the nonmotile *E. coli* may travel from the vagina, rectum, and vulva to the bladder. A nidus of survival for both organisms may be in Skene's glands.[18] In this presentation, discussion has been limited to one bacterium, *E. coli,* for purposes of simplicity only. Other organisms, particularly the streptococcus and staphylococcus, are often also intimately associated with *T. vaginalis* and may be responsible for cystitis either alone or as part of a mixed infection.

It might be well to note that in pregnancy the two diseases discussed in this paper, *T. vaginalis* vaginitis and bacterial infections of the urinary tract, have an increased incidence and pathogenicity.

Summary

1. Of 45 patients with *T. vaginalis* infections, 38 had parasites in the vagina and 40 had parasites in the urethra; 33 had parasites in the vagina and in the urethra, 5 had parasites only in the vagina, and 7 had parasites only in the urethra. In many instances, when parasites were present both in the vagina and the urethra, they were more numerous in the urethra. This localization of *T. vaginalis* in the urethra may be an important factor responsible for recurrence of *T. vaginalis* vaginitis.

2. Case reports suggest a relationship between *T. vaginalis* vaginitis and recurrent cystitis caused by *Escherichia coli* and other bacteria. It is possible that bacteria are transported to the bladder by *T. vaginalis.*

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Technical studies were done by Mrs. Wanda Wolinska and Mrs. Alice Möller.

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SPECIFIC THERAPY FOR VAGINAL MYCOSIS*

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IN SEPTEMBER, 1949, Hesseltine and Beckette[1] made a report on a specific treatment for vaginal mycosis. Credit for the success was given to a 3 per cent concentration of ricinolic acid in a buffered acid gel. A few days before the galley proof arrived it was ascertained that oxyquinoline in 0.5 per cent concentration had been added as a preservative. This step was made by the pharmacist in charge of compounding and without consultation. A footnote was appended to the report stating that this fact confused the point on whether it was ricinolic acid, oxyquinoline, or a combination of the two that had given the very favorable fungicidal results. The initial steps were described in detail in the original paper, but even so some were repeated in this study for further control.

Over a number of years, in laboratory investigations, various types of compounds have been used in a search for a satisfactory fungicide for vulvar and vaginal mycosis. The hydrogen ion concentration had been at one time considered important. Noonan working with us[2] studied the growth rate of the *Candida albicans* in glucose broth in hydrogen ion range from 2.5 to 9.5. The environment was unfavorable at pH of 2.5 and pH 9.5. Moderate growth occurred at the pH of 3.5 and 8.5. As fermentation took place the pH was reduced at each test evidently by the acid production of fermentation until the range of 3.5 to 4.5 was attained. The *greatest growth occurred* in the range of 4.5 to 6.5 pH. This emphasized that acid and alkaline environments were therapeutically valueless as judged on this premise. These findings are in accord with the concepts of the metabolic behavior of these fungi. Accordingly an acid is a by-product of the fermentation.

A number of workers have reported on the in vitro influence of a large number of inorganic and organic compounds. By the usual laboratory standards a number loomed promising. Several of these lost much or all of their fungicidal promise when human serum and blood cells were added to the test solutions. Those that survived these tests were then given in vivo trial. This clinical application yields negligible or poor responses for most of the compounds. Consequently, when the preparation reported in 1949 was found therapeutically efficacious it was believed at the time that ricinolic acid was the responsible agent, for all other tested ingredients had been eliminated except for oxyquinoline. In the original work a culture which had been identified by the number 6225 had been the standard strain for tests for a number of agents. It had retained its typical cultural and morphological character-

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istics. This strain revealed definite but not complete susceptibility to ricinolic acid on a five-minute time exposure as previously described. After the publication of this report the company which had cooperated in the study and had supplied all the material informed us that its strains of *Candida albicans* did not show much susceptibility in vitro to ricinolic acid. It is an established fact in the field of microbiology that an occasional strain may behave peculiarly.

TABLE I. FIVE NEWLY ISOLATED CANDIDA ALBICANS TESTED FOR SUSCEPTIBILITY TO OXYQUINOLINE, RICINOLIC ACID, AND A COMBINATION OF THESE TWO*

AGENT	% SOL.	STRAINS FROM PATIENTS				
		B	S	H	G	P
Oxyquinoline	5	0	0	0	0	0
	3	0	0	0	0	0
	2	0	0	0++	0	0
	1	0	+++	++++	0	0+++
Ricinoleic acid	3	+++	++++	++++	++++	+++
Ricinoleic acid and oxyquinoline	3 0.5	+	++	++++	0	+

*Tests were run in duplicate and with controls. The controls were graded ++++ as full growth and no growth 0, with variations between as +++, ++, and +. Glycerine was the vehicle. Experimental exposure time was five minutes.

With these facts present, five cultures of *Candida albicans* (Table I), all of which had been isolated recently from patients with an active vaginal mycosis, were tested in duplicate against ricinolic acid. All of these five cultures were identical culturally and morphologically. These strains were identified by letter as B, G, H, P, and S. It will be noted that a moderate variation occurs in fungicidal potency in this group. Both the resistances and susceptibilities were distinct. It seems on this chart that oxyquinoline was the more efficient agent. Even so, the concentrations are greater than clinically advisable.

TABLE II. FIVE STOCK CULTURES TESTED THAT HAD BEEN USED OVER A PERIOD OF A MONTH IN TESTS AND FOUND STABLE IN CHARACTERISTICS*

AGENT	% SOL.	NO. 57	NO. 69	NO. 70	NO. 71	NO. 753
Oxyquinoline	5	0	0	0	0	0
	3	0	0	0	0	0
	2	0	0	0	0	0
	1	0	0	+1	0+-	0+
Riconilic acid	3	++++	+++ ++++	+++ ++++	++++	++++
Oxyquinoline and ricinolic acid	0.5 3	0+++	+ ++	+ ++	+ ++	0

*The susceptibility rates to oxyquinoline, to ricinolic acid and to a combination are presented. Tests were run in duplicate and with controls. *Exposure time was five minutes.* The vehicle was glycerine. The controls were graded ++++ for full growth and no growth = 0. The variations between were noted as +++, ++, +.

After this exploration, "stock" strains (Table II) which had been kept for some time were subjected to the same tests. These were also medical Monilia or *Candida albicans* and were identified as Nos. 57, 69, 70, 71, and 735. The results in this group were fairly uniform yet somewhat similar to the ob-

servations noted in a recently isolated strain. Thus quite by accident the strain 6225 had a particular susceptibility to ricinolic acid. In view of these conflicting findings, the outstandingly favorable clinical results are difficult to explain unless there is some factor or factors present in the vagina which enhance the therapeutic result of ricinolic acid.

Perhaps it should be pointed out that ricinolic acid is a derivative of *Palma Christi* or the castor oil plant. Ricinolic acid is obtained from the decomposition of the glyceride and has the appearance of a viscid oil. This viscid oil will solidify below 0° C. It will not solidify in contact with the air in the presence of oxyquinoline for the latter is not homologous with oleic or other acids present in castor oil. Larson and associates[3, 4, 5] showed that when the surface tension of culture media was lowered inhibition of growth of many bacteria resulted. Larson and his co-workers showed also that one of the best agents for this process was soap made from castor oil or a solution of sodium ricinoleate. He also found that sodium ricinoleate had the property of detoxifying bacterial toxin and he felt that this was based on a probable absorption phenomenon. There have been other theories for this phenomenon by Reasoner[6] and Spencer.[7] These details are beyond the scope of this paper, however.

The preliminary series of 98 comprised the first group of patients who were studied for therapeutic fungicidal values. The diagnosis of vaginal mycosis was based upon clinical and microscopic evidence of fungous infection. Three groups of therapies were used for this study: (a) 0.5 per cent oxyquinoline, (b) 3 per cent ricinolic acid, and (c) a combination of (a) and (b). These findings of this study were subsequently supported by the clinical response to the commercial preparation known as Aci-Jel-Improved* in a series of over 400 patients. The number for this controlled study totaled 411 (70, 125, and 118, respectively, for a, b, and c above).

Oxyquinoline sulfate was employed as a preservative in 0.5 per cent concentration. Greater strengths did produce slight irritation in some patients in the preliminary survey. Thus oxyquinoline was used in 0.5 per cent strength in an identical gel. Admittedly greater concentrations might yield better results but also irritation would be encountered. Oxyquinoline is a crystalline yellow powder, readily soluble in water. By the usual standards its phenol coefficient would be classified as considerably inferior. When tested for fungicidal potency in vitro the results are outstandingly impressive. This constituted the other medicament for the study (Table III). The number of patients carried through without the necessity of transfering to other therapy was small. Only 70 patients had been treated sufficiently long to arrive at a clinical conclusion. Treatment was interrupted either because the patients failed to obtain symptomatic improvement or the local conditions failed to improve. All of these patients were treated for at least three weeks or more. Of these 70 cooperative patients, clinical cures were observed in only 24, or 34 per cent. The failures numbered 46, or 66 per cent. Thus these data run contrary to the promise of the laboratory tests for fungicidal effectiveness.

*A product of Ortho Pharmaceutical Corporation.

TABLE III. RESULTS OF OXYQUINOLINE SULFATE (0.5 PER CENT) IN THE TREATMENT OF VAGINAL MYCOSIS CAUSED BY CANDIDA ALBICANS

NUMBER		CURES			FAILURES		
		TREATMENT		TOTAL	TREATMENT		TOTAL
Obstetric	58	3 weeks	6	18	3 weeks	10	40
		4 weeks	3		4 weeks	9	
		1-2 months	9		1-2 months	18	
					2-3 months	2	
					3-4 months	1	
Gynecologic	12	3 weeks	4	6	3 weeks	3	6
		4 weeks	1		4 weeks	1	
		8 weeks	1		8 weeks	2	
Total	70			24 (34%)			46 (66%)

A total of 125 patients received only 3 per cent ricinolic acid in a buffered gel. Approximately 5 c.c. of the material was placed well up in the vagina as previously described. Abstinence was urged. Douches were eliminated. The symptoms of pruritus were completely gone or improved in 120 patients (Table IV). The failure of cure in 5 might be charged to the patient's lack of cooperation by irregular treatment. This yields a 96 per cent cure rate. Clinical response was evident usually within the first few days, although the rate of response varied moderately. Most of those patients who received the material beyond the fourth week were test patients for tolerance. No incidence of intolerance became evident. From a clinical viewpoint treatment might have been discontinued earlier. The 5 classified as failures deserve some attention. Some patients are prone to discontinue therapies as soon as the major symptoms vanish. Such practice allows an exacerbation of the process.

TABLE IV. RESULTS OF 3 PER CENT RICINOLIC ACID IN THE TREATMENT OF VAGINAL MYCOSIS CAUSED BY CANDIDA ALBICANS

NUMBER		CURES			FAILURES		
		TREATMENT		TOTAL	TREATMENT		TOTAL
Obstetric	96	2 weeks	1	91	1 month	3	5
		3 weeks	8		2 months	1	
		1 month	29		3 months	1	
		1-2+ months	58				
Gynecologic	29	3 weeks	4	29			0
		4 weeks	7				
		1 month +	18				
Total	125			120 (96%)			5 (4%)

It is an old observation that recurrence of the mycosis can occur. This must be recognized as the result of favorable conditions of the vagina during pregnancy and especially if the patient is a "carrier."

The patients divided into groups of 96 obstetric and 29 gynecologic. The fact that all 29 gynecologic patients had clinical cures should not be interpreted too enthusiastically.

A combination of ricinolic acid and oxyquinoline sulfate (0.5 per cent) (Table V) was administered to 118 obstetric and gynecologic patients. This series divided into 88 obstetric and 30 gynecologic patients. The failures were

4 in the gravid and 2 in the nongravid group. Thus with 6 failures in 118 it still gives a cure rate of 95 per cent. The duration of treatment was maintained perhaps longer than necessary for two reasons: (1) to ensure adequate time for therapeutic results and (2) to test patient tolerance to the product.

TABLE V. THE RESULTS OF RICINOLIC ACID (3 PER CENT) AND OXYQUINOLINE SULFATE (0.5 PER CENT) IN THE TREATMENT OF VAGINAL MYCOSIS CAUSED BY CANDIDA ALBICANS

		CURES			FAILURES		
NUMBER		TREATMENT		TOTAL	TREATMENT		TOTAL
Obstetric	88	3 weeks	8	84	2 months	2	4
		4 weeks	14		3 months	1	
		Over 4 weeks	66		4 months	1	
Gynecologic	30	2 weeks	2	28	2 months	1	2
		3 weeks	4		3 months	1	
		4 weeks	10				
		Over 4 weeks	14				
Total	118			112 (95%)			6 (5%)

It has been demonstrated that the *Candida albicans* may be present in the carrier state in the vagina. A fair percentage carry these strains in the gastrointestinal system. Since the vaginal flora is related in part to the lower bowel, perhaps this fungous organism spreads readily to the vagina. Since pregnant patients or postmenopausal patients on substantial estrogen therapy are more likely to have vaginal mycosis and since the vaginal mucosa has more glycogen-like material under these circumstances the *Candida albicans* are "opportunists." This contention could be further emphasized by the nature of mycotic vulvitis in the diabetic patient.

The cooperation of the patients (both private and service patients) remained at a high degree. If there were any differences in the extent of cooperation, those of the private patient group excelled.

There were no corrections or deletions of patients in this entire study except those who moved out of the city or transferred to other physicians in the city. Obviously these could not be counted either as cures or failures, for the maintenance of therapy would not be uniform nor would the follow-up be accurate and complete.

The few patients who did not follow directions explicitly and obtained poor results were placed in the failure group.

In clinical application under these conditions ricinolic acid became an efficient fungicidal agent. On the other hand, oxyquinoline did not possess fungicidal action in clinical application upon vaginal mycosis. The presence of oxyquinoline with ricinolic acid did not impair or limit the latter's action. Thus the presence of oxyquinoline as a preservative offered stability to the ricinolic acid in this gel form. The full explanations for this unexpected result between the laboratory and clinical observations remained obscure. The most likely answer is that some specific point of metabolism of the fungi in vivo differs from that in vitro. It is well known that an occasional strain of organism will behave differently than another of the same species. Had the first studies been on a different strain of *Candida albicans* it is unlikely that ricinolic acid would have been applied clinically. The usual variation be-

tween in vitro and in vivo observations must be considered in the evaluation of all new and perhaps some old agents. Thus, some of the compounds which were discarded in the past because of observations in the laboratory need not be assumed to be entirely valueless.

The agents or compounds should be nontoxic and nonirritating. The vehicle should be nonstaining and noninjurious to clothing, furniture, and office floors. The product must be esthetically acceptable.

In addition to these 411 patients, well over 400 others with vaginal mycosis from the general and the private services have used under medical direction the commercial product of ricinolic acid and oxyquinoline of the same proportions as given above with most satisfactory results and without evidence of intolerance.

Vulvar mycoses have been treated with the same materials by application locally and vaginally. Since a good percentage of these patients are diabetics, this medical condition should be treated adequately and properly at this same time. Vulvar mycoses were not included in this study.

Summary

Ricinolic acid in 3 per cent concentration in a tragacanth acacia gel base produced 96 per cent cures (a failure incidence of 4 per cent). Unless there is good cooperation on the part of the patient, the failure rate will increase. This point of cooperation applies to all therapies and especially in instances where the patient must be relied upon to do self-administration. Oxyquinoline in 0.5 per cent concentration yielded an unexpectedly high failure rate of 65 per cent. A combination of 3 per cent ricinolic acid and 0.5 per cent oxyquinoline gave equally good results as ricinolic acid alone (95 per cent cures). Because a "preservative" (oxyquinoline) gave greater stability to ricinolic acid, such a combination is desirable. The same percentages were used in this study for comparison with the previous report.

It can be stated that under the conditions of this study with the concentration of 3 per cent ricinolic acid and 0.5 per cent oxyquinoline, a most satisfactory fungicidal agent for *Candida albicans* infection of the vagina was available.

I wish to acknowledge the willing help and assistance of the house staff and all of the departmental members.

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POTASSIUM PERMANGANATE BURN OF THE VAGINA FOLLOWED BY BOWEL OBSTRUCTION*

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POTASSIUM permanganate instilled locally into the vagina for the purpose of causing an abortion results in a severe necrosis and hemorrhage. The literature frequently refers to these lesions as burns. Since Schull[1] in 1941 presented seventeen cases of vaginal burns produced by the use of potassium permanganate as an abortifacient, there have accumulated several reports of similar nature with various and some severe consequences. McDonough[2] presented sixty-five cases with serious bleeding in 1945. Jetter and Hunter[3] reported two fatal cases in 1949. Both of these patients who died had hemorrhagic necrosis of the uterus, pigmented casts in the tubules, and alkaline methemoglobin in the serum. Lubin and Waltman[4] in 1951 reported upon ten patients with severe vaginal hemorrhage. Carney,[5] in 1953, reported twenty cases, one with the findings of an acute homologous serum jaundice. Recently Alment and Nicol[6] in England reported five such cases of vaginal hemorrhage. Steward and Webster[7] from the Cook County Hospital of Chicago reported twenty-three cases of serious hemorrhage in 1954 from the use of this chemical. From the foregoing data we can conclude that the use of potassium permanganate douche or tablet insertion as an abortifacient has resulted in an increasing number of vaginal burns and hemorrhages with severe complications.

We are herewith presenting a case that portrays the far-reaching consequences that may follow this ill-advised use of potassium permanganate.

A 29-year-old Negro woman, gravida iii, para ii, who last menstruated on Nov. 26, 1952, entered the Mount Sinai Hospital on Feb. 28, 1953. She had profuse intermittent vaginal bleeding with explusion of clots for five days, and severe abdominal cramps that began five hours prior to hospital admission. A physical examination revealed moderate bleeding from the vagina; her temperature was 98.6° F., blood pressure 90/45, pulse 100 and weak, and respirations 22 per minute. Vaginal examination revealed a soft mass, 3 cm. in diameter, purplish in color, which was believed to be fetal tissue in the process of abortion. The uterus was soft and about the size noted at fourteen weeks of gestation. A blood study revealed the following: the erythrocyte count was 2.2 million per cubic millimeter, hemoglobin was 6 Gm. or 38.4 per cent, and the leukocyte count was

*Presented at a meeting of the Chicago Gynecological Society, Feb. 19, 1954.

18,500. The patient was immediately given 500 c.c. of whole blood. She was then taken to the operating room. When the vault of the vagina was properly exposed, a necrotic mass was observed in the region of the right lateral portio vaginalis uteri. Above this, near the apex of the vaginal vault on the right side, there was a circumscribed area where the vaginal epithelium was absent. Brisk bleeding, apparently from an eroded vessel, came from this denuded area. The necrotic mass was removed and hemostasis secured by interrupted sutures. Gross and microscopic examination of tissue removed revealed inflammation and necrosis. When the patient was later questioned she denied any intent to cause an abortion and stated that she had used "purple pills" in a douche bag—about four or five pills with each douching. These pills were later identified as potassium permanganate.

The next day the patient complained of pain in the upper half of the abdomen. On the third day, she stated that the abdominal pains were increasing. The abdomen was moderately distended and the history of no bowel movements for four or five days was elicited. The patient was given an oil retention enema and mineral oil with no results. On the fourth hospital day no bowel sounds were noted. Roentgenographic study confirmed a diagnosis of paralytic ileus. Levine suction was started and 3,000 c.c. of intravenous fluids was given. The abdomen became subsequently much more distended despite the insertion of a Miller-Abbott tube. Intravenous fluids, antibiotics, and prostigmine were all administered. The bowel sounds were always present but diminished. On the seventh postoperative day a magnesium sulfate, glycerin, and water enema was given which resulted in a copious expulsion of feces and flatus but on the next day the patient became severely distended once more. The Friedman modification of the Aschheim-Zondek test became positive at this time. A rectovaginal examination on the twelfth hospital day revealed marked tenderness and some infiltration of the parametrium and cul-de-sac.

A diagnosis of pelvic cellulitis and peritonitis was the working diagnosis at this time. On the fifteenth hospital day, bowel sounds were of normal frequency but high pitched. Mineral oil by mouth had not passed through for the past three days. The following day, the diagnosis of a probable mechanical obstruction was made and an exploratory laporotomy was performed. A generalized peritonitis, stemming from the cul-de-sac and going up both lateral gutters, was noted. The small bowel was kinked and matted together in a large mass over the left lower quadrant. The descending colon revealed a large necrotic area and the continuity of the colon could not be followed. Adhesions of the small bowel were lysed; drains were inserted above the necrotic area and the incision closed. A transverse colostomy was then performed. The patient had a stormy, febrile postoperative course but left the hospital thirty-three days after her admission, in good condition with a functioning colostomy and the pregnancy still intact.

The patient was referred to the prenatal clinic and it was noted that, as the pregnancy progressed, the colostomy developed an eversion that became marked. On Aug. 27, 1953, the patient was again admitted to the Mt. Sinai Hospital for an elective cesarean section because of herniation of the colostomy, and induration noted in the right lateral fornix of the vagina, the original site of the potassium permanganate burn. A low cervical cesarean section on Aug. 28, 1953, resulted in the delivery of a normal male infant. At the same time the site of the obstructive lesion was explored and the tissue was now noted to be normal. The numerous dense, fibrous adhesions binding the small bowel to the abdominal wall were severed. The postoperative course was uneventful. This patient was admitted for a third time on Nov. 2, 1953, and the colostomy was closed, after an investigation by proctoscopy and x-ray had revealed the bowel to be patent. Again the patient had an uneventful postoperative course and was sent home on the twelfth postoperative day, with the colostomy opening eliminated and the bowels again functioning normally.

In view of the frequency of potassium permanganate burns and the serious complications, it is our belief that legislation should be enacted that will prohibit the sale of this drug without a physician's prescription.

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PLACENTA INCRETA

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PLACENTA accreta is a rare complication of labor, somewhat over 200 cases being recorded in the literature up to 1953.[1] It is characterized, clinically, by a total or partial failure of placental separation. Pathologically, there is an absence of the decidua basalis with myometrial invasion by the chorionic villi.

Placenta accreta has been divided into focal, partial, and complete types. This classification is based upon the surface extent of placental attachment. In addition, a secondary classification is based upon the depth of trophoblastic invasion of the myometrium. If the chorionic villi have completely penetrated the serosa of the uterus, the condition has been named placenta percreta. Invasion limited to the uterine wall has been termed placenta increta.

The reports of incidence of placenta accreta vary. Irving and Hertig[2] reported its occurence once in 1,956 deliveries.[2] Phaneuf,[3] in a review of 10 reports in the literature, noted an average incidence of 1 in 14,622 deliveries. Eastman[4] did not note a single instance of the complete type in over 70,000 deliveries. We are reporting the first case at the French Hospital in 25,000 deliveries.

Numerous etiological factors have been held responsible for the development of this rare complication. Irving and Hertig,[2] in reviewing 86 cases, found 37 instances in which possible etiological factors could be determined. These include previous manual removal of the placenta, dilatation and curettage, and a previous history of endometritis. Parks and his associates[5] add submucous fibromyomas, uterine scars, and possibly adenomyosis. Kistner and co-workers[6] stressed a high coincidence of placenta accreta and placenta previa.

A case report follows in which several possible etiological factors were present.

Case Report

Mrs. S. R., a 29-year-old white woman, gravida v, para ii, was admitted to French Hospital Oct. 15, 1953, on the service of Dr. Speiser, with a history of painless vaginal bleeding of one hour's duration, described as "considerable." The estimated date of confinement was Jan. 29, 1954. The previous obstetrical history revealed that the patient had had a full-term uneventful delivery in 1947. In 1948 spontaneous abortion of a 2½ month fetus occurred, requiring curettage. In 1949 the patient suffered another spontaneous abortion at 2 months. In 1950, three weeks following full-term delivery, a curettage was performed for retained secundines.

At the time of admission the uterus was enlarged to the size of a 6½ months' gestation. The fetal heartbeat was 156, regular and strong. Hematological data showed a mild anemia with a normal coagulogram.

The patient had dark brown vaginal staining unaccompanied by pain for the next 4 days. Placentography showed a low implantation of the placenta. The patient was discharged to be followed closely as an outpatient.

Four days following her discharge, she was readmitted with almost continuous brown vaginal staining followed by a small gush of bright red blood just prior to entrance to the hospital. The physical examination was unchanged. The patient continued to have dark brown vaginal staining unaccompanied by pain for the next 11 days, following which there was a cessation of vaginal staining. She was again discharged.

The patient was readmitted 3 days prior to her estimated date of confinement because of the previous history of vaginal bleeding. There had been no further vaginal bleeding since her discharge from the hospital. Three days after admission to the hospital, slight bleeding from the nose and gingival areas occurred, as well as scanty vaginal spotting. A bleeding tendency was suspected, but complete hematological workup, including clot observation tests, was normal. At 1:40 A.M. on Jan. 23, 1954, the patient was awakened by irregular uterine contractions, followed shortly by a sudden gush of bright red blood per vaginam, which was estimated at 350 c.c. Rectal examination disclosed the cervix to be completely effaced and 2 cm. dilated. A diagnosis of premature separation of the placenta was made. An infusion of 1,000 c.c. of 5 per cent glucose in water with 1 c.c. of Pitocin was started, following which labor made rapid progress. Blood was replaced. After a rapid labor of 1 hour, 45 minutes, the patient was delivered spontaneously of an 8 pound, 2 ounce, living male child in good condition. Immediately following the end of the second stage, there was a sudden gush of blood from the vagina estimated at 800 c.c. Pelvic examination disclosed that the placenta was only partially separated, and could not be expressed by the Brandt maneuver. Intrauterine palpation of the remaining portion of the placenta showed that a part of it was intimately attached to the anterior wall. An attempt at manual removal was only partially successful. The area of attachment felt very ragged; the myometrium in this area was thin and friable. A diagnosis of partial placenta accreta was made. The bleeding continued briskly. The uterine cavity and vagina were packed preliminary to hysterectomy. As expected, the packing proved to be ineffectual in controlling hemorrhage, but blood replacement was adequate. Under general anesthesia, a subtotal hysterectomy was quickly performed. The surgical procedure was complicated by a hematoma of the left infundibulopelvic ligament which necessitated a left salpingo-oophorectomy. The estimated blood loss up to this time was 3,000 c.c., all of which had been replaced. The immediate postoperative course was good. About three hours post hysterectomy shock developed and the patient received an additional 1,000 c.c. of whole blood. A sterile vaginal examination disclosed a hematoma of the left broad ligament, which was treated conservatively with blood replacement. The hematoma proved to be self-limited and the patient improved slowly. The subsequent postoperative course was complicated by spiking temperatures for the first three days, lowered hemoglobin, and a moderate ileus. Therapy consisted of massive doses of antibiotics, whole blood transfusions, and restoration of electrolytic balance. The patient was discharged on the twelfth postoperative day in good condition. Vaginal examination just prior to discharge showed the presence of a firm, slightly tender mass, 8 by 15 cm. in the region of the left adenexa.

Pathological Report (by Dr. Cyril Solomon).—

Gross: The specimen consisted of the postpartum supracervically amputated uterus which measured 14.5 cm. from the fundus to the internal os, 11.5 cm. across the fundus, and 6 cm. anteroposteriorly. There were multiple, white, glistening, well-encapsulated nodules measuring up to 0.5 cm. in diameter noted in the subserosa.

The myometrium measured up to 3.5 cm. in thickness. The lining of the uterine cavity was roughened, grossly hemorrhagic, and in the region of both cornua there were several smooth, glistening, succulent, polypoid areas. Four centimeters above the level of the internal os there was a pedunculated mass of tissue containing blood clot and fibrous strands measuring 2.2 by 4 cm. This mass was intimately attached with no specific cleavage plane.

Fig. 1.

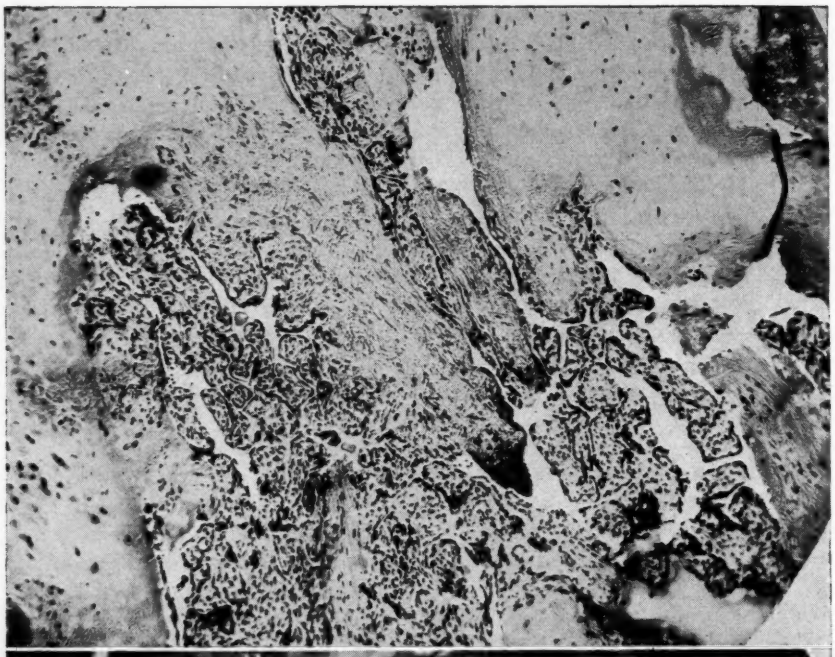
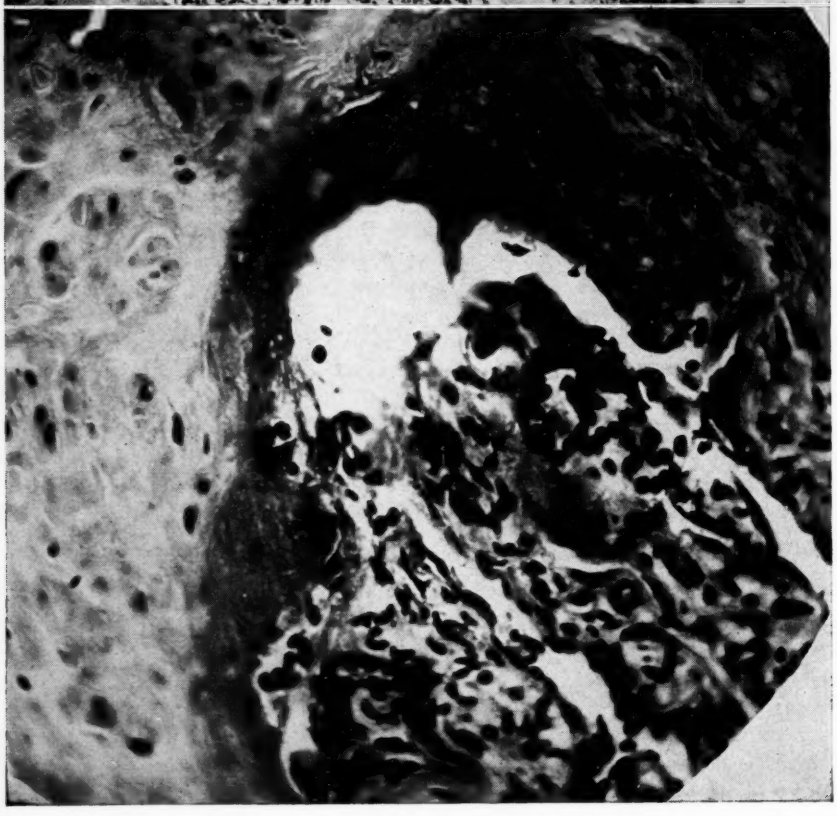


Fig. 2.



Microscopic: Multiple sections of the polypoid hemorrhagic material seen in the wall showed invasion of the musculature by placental tissue. This was apparent with both the hematoxylin and eosin and trichrome stains. The placental tissue went into the succulent and edematous muscle of the uterus and was found around extremely dilated blood vessels. There was a mild lymphocytic reaction in several sections. There was no evidence of old scar formation in the area of implantation of the placental tissue. The decidua basalis was absent.

Diagnosis: Placenta increta, focal; myomas of the uterus, subserous.

Comment

Of the various etiological factors said to be associated with the development of placenta accreta, two were noted in this case—previous curettage and a low implantation of the placenta.

In focal or partial placenta increta, the treatment of choice should be immediate hysterectomy with uterine packing only as a temporary expedient. Schumann[7] considered procrastination and conservative therapy for the young primigravida.

Summary

A case of placenta accreta, focal increta type, is reported.

This case illustrates two etiological factors previously recorded in the literature.

Rapid subtotal hysterectomy is the treatment of choice.

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PEPTIC ULCER COMPLICATING PREGNANCY
A Report of Three Cases

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PEPTIC ulcer complicating pregnancy is fortunately an extremely rare occurrence. In 1948 Bernstine and Friedman[1] reported 3 cases and summarized the case that had been previously reported by LeWinn[2] in 1947. In the series reported by Bernstine and Friedman, their cases either suggested or proved the existence of ulcer prior to pregnancy. The following 3 cases are reported because of the freedom from ulcer symptoms prior to the onset of pregnancy, and because of the severe hemorrhage in one patient.

CASE 1.—Mrs. R. O. was a 23-year-old graduate nurse who was first seen on Nov. 12, 1950, and stated that her last menstrual period had been Sept. 25, 1950. The anticipated date of confinement was July 3, 1951. Her past history was relatively innocuous except for painless hematuria of six to seven months' duration. She was admitted to the Massachusetts General Hospital on Dec. 4, 1950, and discharged on Dec. 8, 1950. The diagnosis at this time was simply hematuria with question of etiology. The urine showed no albumin, no white cells, and no casts, and 5 to 7 red cells per high-power field. Intravenous pyelogram was normal. Cystoscopic examination showed a mild cystitis of the trigone with a possible granulomatous mucosa at the right ureteral orifice. Retrograde pyelogram was negative. Separate examinations of the urine were negative. An old tuberculin test 1:10,000 was reported as negative.

Her family history is interesting because of a subtotal gastrectomy which had been performed on her father in 1951 because of a duodenal ulcer.

The patient's prenatal course was perfectly normal with no history of heartburn, gas, indigestion, or nausea at any time. On Feb. 2, 1951, the patient called and stated that she had had a massive bout of hematemesis and melena. The patient stated at this time that she felt extremely weak and was unable to stand. She was admitted to St. Elizabeth's Hospital by ambulance where she presented the appearance of a woman who has had an acute loss of blood. The red blood count was 2.3 million, hemoglobin 8.4 Gm. per 100 c.c. of blood, and hematocrit 23 volumes per cent. The prothrombin time was 14 seconds with a control of 14 seconds. The bleeding time (Lee-White) was 2 minutes and clotting time 2 minutes. Upon admission she was given three transfusions of 500 c.c. of whole blood. The patient was Rh negative and she was given 3 pints of Rh-negative, type O blood, with A and B substance added. The fourth transfusion was stopped after approximately 100 c.c. of whole blood had been administered because of chills and the appearance of hives. She was seen in consultation by Dr. Richard Stanton who suggested that because of the sudden onset of bleeding and the paucity of symptoms prior to the onset of the bleeding, he felt it would be advisable to observe the patient further. On Feb. 11, 1951, the patient had stopped bleeding, and x-ray examination at this time showed an active duodenal ulcer. She continued to show improvement although, following the admission to the hospital, she began to notice heartburn and epigastric distress. She was placed on a gradually increasing Sippy diet and was discharged on Feb. 18, 1951, with a diagnosis of active duodenal ulcer. On discharge from the hospital the hemoglobin was 10.1 Gm. and the hematocrit 32.

She was seen again on Feb. 28, 1951, at which time her blood pressure was 130/80, and she was symptom free except for severe heartburn. Because of the heartburn and the known ulcer, it was felt that Banthine, 100 mg. every 6 hours, might improve her symptoms. She followed this regime from March 22, 1951, until June 13, 1951. The heartburn was successfully relieved with Amphojel. On March 29, 1951, an x-ray showed a nonobstructing duodenal deformity due to an inactive duodenal ulcer. On June 13 she was seen and claimed that the Banthine had caused considerable discomfort particularly with dryness and a "heavy feeling" in her stomach. Banthine was accordingly discontinued and the patient was placed on Amphojel by mouth. On May 23, 1951, an Rh antititer was reported as negative in both saline and albumin, and the Coombs test was reported as negative.

On July 3, 1951, she was admitted to St. Elizabeth's Hospital at 2:00 A.M. in strong active labor with three- to four-minute pains. At 2:48 P.M. she was delivered by low forceps under spinal anesthesia of a 7 pound 7 ounce male infant whose cord blood and hematology showed no evidence of erythroblastosis. The patient had an uneventful postpartum course and was discharged on July 10, 1951. She was seen again on Sept. 5, 1951, at which time she was free of any ulcer symptoms. The postpartum hematocrit was 37, with a hemoglobin of 11.2 Gm.

The patient subsequently had two recurrences of severe hematemesis, and in February of 1952 was admitted to St. Elizabeth's hospital where a subtotal gastrectomy was performed. She made an uneventful recovery and has been well since.

CASE 2.—Mrs. A. O. was a 28-year-old gravida iii, para ii. Her past history was negative other than for an appendectomy in 1944 and pyelitis at 11 years of age for which she was hospitalized for three weeks.

Her past obstetrical history is extremely interesting. The first pregnancy in 1948 was characterized by mild heartburn and an occasional bout of gas and nausea and vomiting. On March 12, 1948, however, she complained that mild hematemesis had occurred the previous day with a "choking sensation" in her throat. At this time she stated that she had vomited several times and felt that the hematemesis was due to severe retching. She was unable at this time to state exactly how much she had vomited. On March 26, 1948, she went into spontaneous labor and after 20 hours was delivered of a 6 pound, 10½ ounce normal female infant by low forceps. Her postpartum course at this time was symptom-free.

The second pregnancy in 1949 was characterized only by heartburn. There was no history of hematemesis or melena. On March 15, 1949, following a twelve-hour labor, she was delivered by low forceps of an 8 pound 10 ounce male infant and had an uncomplicated postpartum course.

On March 23, 1950, she was seen again, this time complaining of epigastric pain with a "brownish discharge" from the rectum. Because of the bout of hematemesis in 1948 and the present symptoms of epigastric distress, it was felt that the possibility of an ulcer should be considered, and on March 24, 1950, an upper gastrointestinal series and barium enema were done. At this time the esophagus showed no evidence of constriction, dilatation, or irregularity. The stomach was medium low in position, of good tone, with normal peristalsis, free mobility, and no filling defect that would be consistent with carcinoma or ulcer. At the end of six hours, the head of the meal was at the rectum revealing hypermotility and hyperirritability. The small bowel was normal in appearance. The large bowel showed a narrowing of the descending colon consistent with simple colitis.

She was seen for the third pregnancy in August of 1950. At this time she stated that her last menstrual period was July 4, 1950, with an expected date of confinement of April 11, 1951. On August 9, 1950, she complained of mild nausea and vomiting with some heartburn and was given antacid tablets to take with relief of the symptoms. On Jan. 25, 1951, she stated that she had had one day of rectal bleeding. She was unable to say at this time, however, just how much bleeding there was. On Jan. 30, 1951, she stated that she had begun vomiting blood on January 29, and she estimated that she had had approximately 12 episodes of hematemesis. She complained of severe heartburn at this

time. She was admitted to St. Elizabeth's Hospital on Jan. 30, 1951. At this time on admission to the hospital she had severe vomiting characterized by bright red and coffee-ground vomitus and a "choking" feeling in the neck after the first two episodes of bleeding. On January 31, an upper gastrointestinal series was done. At this time the x-ray report read that the duodenal cap did not fill out well and was somewhat deformed, but no ulcer crater could be demonstrated. The pregnant uterus at this time made palpation difficult because it elevated the stomach. The roentgenologist's conclusion, however, was duodenal deformity which might be due to duodenal ulcer.

On Jan. 30, 1951, laboratory work showed a hemoglobin of 10.5 Gm. per 100 c.c. of blood, with a hematocrit of 35 volumes per cent. The prothrombin time was 14 seconds with control of 14 seconds. The blood sugar was 70 and the nonprotein nitrogen 21 mg. per cent, clotting time 12 (Lee-White), and a bleeding time of 3 minutes. Total protein was 6 Gm. per cent with albumin 4.1 and globulin 1.9 Gm. per cent. Examination of the feces at this time showed a trace of occult blood in the stool. She was given nothing by mouth for 24 hours and then placed on antacids and a Sippy diet. She improved rapidly under this regime with no further episode of hematemesis or melena, and she was discharged on a Sippy regime.

On April 10, 1951, she was admitted for induction of labor, and following twenty hours of rather sporadic labor she was delivered normally of a female infant under gas-oxygen-ether anesthesia. She had an uneventful postpartum course and was discharged on the seventh hospital day. On April 16, 1951, an upper gastrointestinal series was done which showed a minimal nonobstructing duodenal deformity secondary to scarring from a probable old ulcer. When seen three months later, she was free from ulcer symptoms.

CASE 3.—Mrs. K. W. was a 30-year-old gravida i, para 0, whose last menstrual period was Sept. 8, 1950, with an expected date of confinement of June 15, 1951. Her past history was uneventful other than for a right oophorectomy performed in 1947. She was first seen on Dec. 28, 1950, at which time she complained of mild indigestion with no other symptoms referable to the gastrointestinal tract. Vaginal examination showed a nulliparous introitus with a fundus approximately 3½ months' size, and the patient was placed on routine prenatal medication. Her prenatal course was uneventful with no reference to gastric disorder other than mild nausea and occasional vomiting until May 3, 1951, at which time she complained of severe heartburn. In addition, she also complained of pain after eating. It was decided to treat her symptomatically, and she was placed on 100 mg. of Banthine every 6 hours and ½ ounce of Amphojel every 4 hours, with a modified Sippy diet. The heartburn increased in severity, however, and on the following day (May 4, 1951) it was decided to admit her to St. Elizabeth's Hospital for study. On admission she was placed on a Sippy diet and blood chemistry at this time showed a normal nonprotein nitrogen of 24 mg. per cent, normal total protein of 5.6 Gm. per cent, with an elevated uric acid of 6.8 mg. Urine examination was negative, and there was no elevation of blood pressure or edema of the extremities. The blood chlorides were 103 mg., hematocrit 31 volumes per cent, and hemoglobin of 9.1 Gm. per 100 c.c. of blood. An upper gastrointestinal series was performed on May 7, 1951, at which time a duodenal ulcer was demonstrated. She was placed on a convalescent Sippy diet, and the Banthine, 100 mg. every 6 hours, was continued.

In spite of the diet and the Banthine, she continued to be severely nauseated with vomiting, and complained almost constantly of heartburn. However, at her own request she was discharged on May 10, 1951. She was seen again on May 11, 1951, at which time she was feeling somewhat better, was taking Dramamine in an attempt to control the nausea, and was still on the Banthine.

On May 18, 1951, she complained of severe nausea with mild vomiting, although she stated that the heartburn had improved. Vaginal examination at this time showed that the cervix was anterior, 1½ fingers dilated, and soft, and the vertex was floating. Because of the floating head, it was decided that expectant treatment should be followed. On May 25, she was seen again and stated that the nausea and vomiting had diminished

and that she had noticed some decrease in the heartburn. Examination at this time showed that the cervix had not changed although the vertex was now dipping in the inlet. On June 1, 1951, she went into spontaneous labor, and following a rapid six-hour labor, she was delivered of a 7 pound, 5 ounce male infant under spinal anesthesia. She was discharged from the hospital on June 8, 1951.

On June 29, 1951, a repeat upper gastrointestinal series showed no evidence of duodenal ulcer. The Banthine was discontinued, and the patient was placed on a regular diet with no ill effects.

She was seen again on Dec. 7, 1951, because of severe vaginal bleeding. Her last menstrual period was October 23, 1951. She was placed on stilbestrol and had an uneventful prenatal course. On July 18, 1952, following a labor of one and one-half hours, she was delivered normally of a 7 pound female infant under gas-oxygen anesthesia. At no time during this second pregnancy did she manifest any symptoms referable to the gastrointestinal tract other than an occasional episode of nausea and vomiting.

The three cases that have been presented have shown three incidences of duodenal ulcer complicating pregnancy. It is probable that more pregnancies are complicated with duodenal ulcers than have been suspected in the past, but because the obstetrician has come to look upon heartburn as a more or less "normal" complication of pregnancy, little attention is paid to it. The two cases in which Banthine was tried for the control of the ulcer symptoms did not respond as well as had been anticipated. Whether this failure of response is due to the side effects of the drug which make it extremely difficult for the pregnant woman to withstand is difficult to say. It seems advisable, however, that patients who complain of constant epigastric distress during pregnancy should be given the advantages of an upper gastrointestinal series to determine whether or not an ulcer is present.

Conclusions

1. Three cases of duodenal ulcer complicating pregnancy have been presented.

2. In the three cases no previous ulcer history could be elicited. In the third case it is obvious that the patient apparently had had ulcer symptoms which could not be definitely proved by x-ray.

3. All patients were treated conservatively and all patients had an uncomplicated labor and delivery followed by an uncomplicated postpartum course.

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DEATH FROM THE EFFECTS OF MYOCARDIAL ISCHEMIA FOLLOWING HEMORRHAGE IN ECTOPIC PREGNANCY

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RECOVERY is common following surgical intervention for the correction of ruptured ectopic pregnancy in patients who suffer variable degrees of blood loss and incident vascular instability. This is borne out by Crawford and Hutchinson[1] in their review of experience in the past decade and a report of 300 cases without mortality. In our experience in the anesthetic management of such cases during the past nine years, 3 patients presenting a similar clinical picture have died following operation. Reference to this type of postsurgical death has not been found in the literature, although Campbell[2] alludes to a case that may be similar. These cases did not occur in the same hospital. All 3 patients were Negroes, which is probably coincidental. All 3 patients received delayed medical attention, which we do not feel is coincidental.

Case Reports

The first case occurred approximately nine years ago. C. M., a 25-year-old primipara, was admitted to the hospital with signs of intra-abdominal bleeding. For reasons not known, the patient was not operated upon until 24 hours after admission. At this time the hemoglobin was less than 10 Gm. and she was in obvious circulatory distress. Cyclopropane-oxygen anesthesia and adequate transfusions with whole blood were administered, so at the end of the surgical procedure the patient was not in shock and was considered in good condition. Her postsurgical course for twenty-four hours was uneventful: She was conscious, rational, and comfortable, urine output was satisfactory, and the hemoglobin 13.5 Gm. twelve hours postoperatively. The patient called for the nurse approximately twenty-four hours postoperatively, complained of acute shortness of breath, and was in obvious difficulty. The ward physician found the patient coughing frothy, blood-tinged sputum and observed moist râles in all lung fields. The patient suddenly died before any treatment could be instituted. Autopsy revealed acute pulmonary congestion and pulmonary edema.

The second such case was seen about five years ago. This 20-year-old patient, L. T., underwent operation less than an hour after admission. She had been ill at home for at least twenty-four hours previously, and was brought to the hospital because she had collapsed. There was evidence of intra-abdominal bleeding and a hemoglobin of less than 10 Gm. She was in shock. Blood transfusion was started and the patient anesthetized with cyclopropane-oxygen. She made an immediate recovery from operation and anesthesia but approximately 10 hours postoperatively, being fully conscious and in no apparent distress, suddenly developed acute pulmonary edema and died within a very few minutes. Autopsy confirmed the presence of pulmonary edema.

The third case occurred recently and led us to conclude that this sequence of events was not without significance and should be considered as a possibility, although uncommon, in cases of ruptured ectopic pregnancy.

This patient, S. J., was a 30-year-old obese woman, para v, gravida vii (two spontaneous abortions). The admission diagnosis was incomplete abortion. The blood pressure was 110/60; pulse 90; temperature 98.6° F.; hemoglobin 11.5 Gm. Two days later dilatation and curettage was performed. On arrival in the operating room, it was noted that she was extremely pale, dyspneic, apprehensive, and apparently in marked distress. The

blood pressure was 80/60; pulse 160; respirations 40; hemoglobin 10 Gm. The abdomen was distended and tender to palpation. Free blood was aspirated on abdominal tap and a diagnosis of ruptured ectopic pregnancy was made. Blood transfusion was begun and two hours later the blood pressure was 110/70, pulse 150, and respirations 30. Induction of anesthesia was accomplished with 50 per cent cyclopropane-oxygen through an oral endotracheal airway. Succinylcholine in a 0.1 per cent drip was used for relaxation. The picture of shock during operation remained unchanged. The blood pressure varied between 90/60 and 130/90 and the pulse rate remained between 150 and 170, although a total of 2,000 c.c. of blood was administered. A ruptured ectopic tubal pregnancy was removed. Fifteen minutes after completion of the operation and while still breathing oxygen, the patient became cyanotic and moist râles were heard throughout both lung fields. Beige-colored frothy sputum was aspirated through the endotracheal airway. The blood pressure was 95/75; pulse 170. In spite of efforts at resuscitation the patient died 26 minutes later. Postmortem examination confirmed the diagnosis of severe pulmonary edema. The estimated blood loss during operation (including free blood clots removed) was 3,000 c.c.

Comment

Since this type of death is uncommon and is not predictable, at best we can only theorize as to the cause. We do not believe the type of anesthesia, although common in each case, was responsible. Recovery from anesthesia in two cases can be considered as complete. Post-cyclopropane circulatory depression was not a factor.

It is believed that the terminal pulmonary edema common to these cases is an example of acute cardiac failure. During the period of blood loss the heart undergoes a period of ischemia with some degree of myocardial damage. When *normal* hemodynamics are accomplished by adequate replacement therapy, the damaged myocardium is capable of accommodating for a variable brief period of time. The resulting pulmonary edema is evidence of acute left-sided heart failure. Careful thought has been given to the possibility of the role of excessive transfusions in these patients. We do not believe this factor played a role in so far as transfusion of a greater quantity of blood than was lost is concerned.

It is believed that this type of case may be better subject to prevention than it is to treatment, although its low incidence of occurrence may make this difficult. It is, however, suggested that any case of prolonged intra-abdominal bleeding be considered as one of myocardial ischemia of unknown severity, and that the principles of preoperative, anesthetic, and postoperative management of patients with cardiac disease are applicable to cases of ruptured ectopic pregnancy when delay in diagnosis and therapy has been present.

Summary

1. Three cases are presented in which death with pulmonary edema followed surgical intervention for ruptured ectopic pregnancy.

2. It is suggested that these deaths are of cardiac origin.

3. Application of the principles of preoperative, anesthetic, and postoperative management of cardiac patients is recommended.

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OVARIAN DYSGERMINOMA AND PREGNANCY*

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DYSGERMINOMA is a rare form of ovarian tumor that may be found at any age, although most often it is found in young girls. It has been reported before childbearing and after childbearing but rarely in the same individual. After a brief discussion of the embryology, we are presenting a case where conservative surgery later permitted a young girl with dysgerminoma to bear a child.

Embryology.—The earliest sex glands develop in close proximity to the mesonephros, or Wolffian body, and of course more anteriorly in the same region the Müllerian ducts appear. The anlage of the sex glands appears very early in fetal development as an aggregation of cells on the medioventral aspect of the Wolffian body, covered by the primitive peritoneal or celomic epithelium.[5] This early undifferentiated phase is soon followed by one in which the cells arrange themselves into sex cords or columns. In the female these soon disappear and further differentiative phenomena make themselves evident as a second group of columns (Pflüger's) with a characteristic grouping of cells. Around the germ cells or oogonia appear rosettes of satellite cells which are the progenitors of the follicular apparatus.

Dysgerminomas[1] are believed to arise from cells which date back to this early undifferentiated phase of gonadal development. In this phase the cells have not as yet acquired male or female characteristics, so that, as might be expected, dysgerminomas have no effect on the sex characteristics of the patient. In Novak's[2] classification of ovarian tumors they are classified in the malignant embryonic or dysontogenetic group along with the granulosa-cell tumors, the thecomas, and the arrhenoblastomas.

Case Reports

E. K., Hospital No. 195450, aged 18 years, a white single Jewish girl, was admitted to the private service of Dr. A. C. Posner on Oct. 7, 1947, because of a mass in the lower right side of the abdomen associated with occasional pain during the previous year and daily pain for the two weeks prior to admission. The menstrual cycles were very irregular and combined with severe dysmenorrhea.

Examination showed a mass present in the right lower quadrant. It was very tender and separate from the uterus. There were no other gross gynecological findings. A preoperative diagnosis of ovarian cyst was made and on Oct. 10, 1947, a right salpingo-oophorectomy and appendectomy were performed.

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A 13 by 9 cm. solid tumor was found at the site of the right ovary. The external surface was pinkish yellow, smooth, and lobulated, and the cut surface was homogenous, yellowish white in color, and firm in consistency.

Microscopic sections showed small nests and cords made up of polyhedral cells with round hyperchromatic nuclei and scant cytoplasm. The cells were separated by abundant, loose, trabeculated fibrous tissue infiltrated with lymphocytes. Multinucleated giant cells were frequent (Fig. 1). The pathological diagnosis was ovarian dysgerminoma. A characteristic slide was sent to the Ovarian Tumor Registry (No. 365) which concurred in the diagnosis. Because of the age of the patient and the fact that the tumor mass was unilateral and well encapsulated with no apparent metastasis, it was decided not to resort to any further surgery at this time.

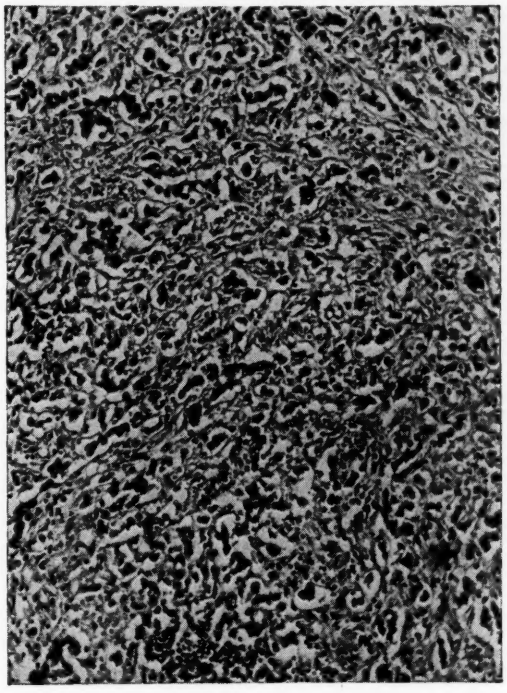

Fig. 1.—(No. 34356) Small nests and cords of polyhedral cells with hyperchromatic nuclei in an abundant, loose, fibrous tissue. (×100; reduced ¼.)

The patient had an uneventful convalescence and was discharged well on Oct. 23, 1947.

On Sept. 3, 1952 (five years after the initial operation) she was delivered of a living 5 pound 5 ounce female infant after a spontaneous labor of three and one-half hours.

In November of 1953 (about one year after the birth of her child) the patient began to notice progressive enlargement of the abdomen and on her second admission (Hospital No. 268579) on Dec. 28, 1953, there was a large, hard, tender abdominal mass extending from the pelvis to the umbilicus. Abdominally it felt like a pregnant uterus. The Frank-Berman test was negative. With the previous pathological report in mind and because of the progression of symptoms it was decided to do a radical operation. On Dec. 30, 1953, a total abdominal hysterectomy and left salpingo-oophorectomy were done. The left ovary was the seat of a solid, encapsulated tumor measuring 20 by 14 by 12 cm. (Fig. 2). The external surface was smooth and nodular with areas of punctate hemorrhage. The cut surface was pale yellow and homogenous. Microscopic section showed large cells of fairly uniform appearance with large nuclei and scanty cytoplasm arranged in nests and cordlike masses. The stroma showed a variable amount of lymphocytic infiltration. The pathological report again was ovarian dysgerminoma (Fig. 3).

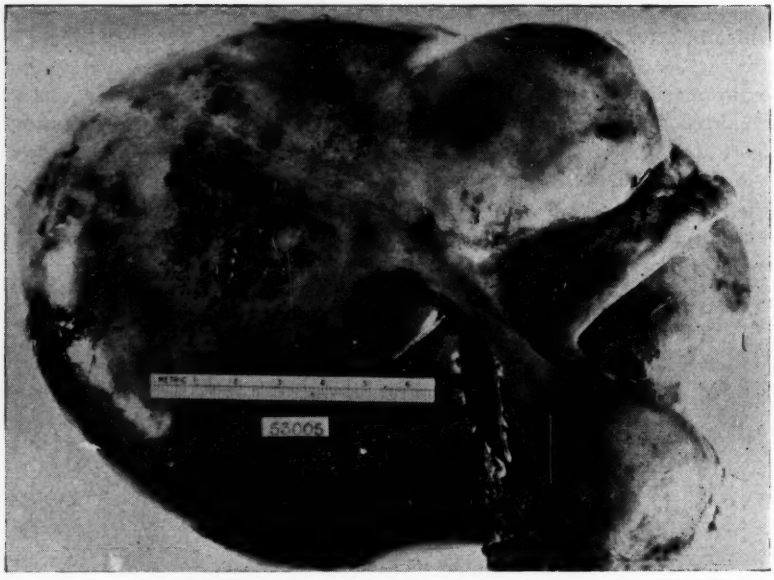

Fig. 2.—(No. 53005) Gross specimen, second admission.

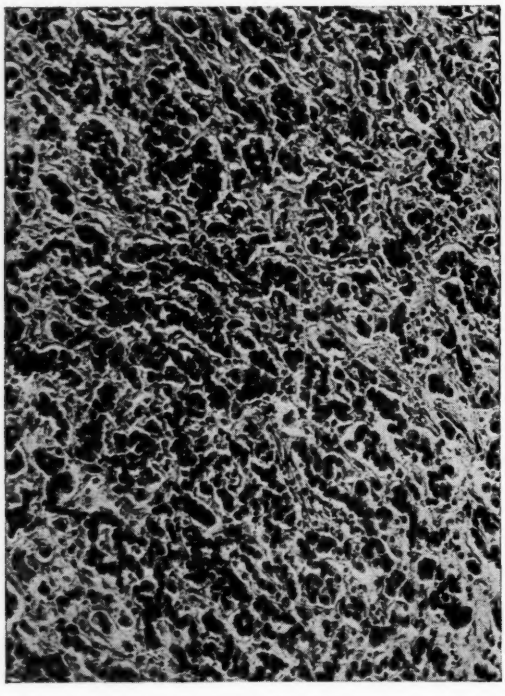

Fig. 3.—(No. 53005) Large cells with large nuclei and scanty cytoplasm arranged in nests and cordlike masses. (×100; reduced ¼.)

Comment

Dysgerminoma occurs about one-third as frequently as granulosa-cell tumors, which make up about 10 per cent of all primary ovarian tumors.[3] The microscopic characteristics are distinctive. These consist of large round,

ovoid, or polygonal cells with large hyperchromatic nuclei arranged in nests separated by a fibrous stroma which is infiltrated with lymphocytes.

There can be no question as to the malignancy of dysgerminomas in general, although there is much variation in individual cases. As a group they are less malignant than the granulosa-cell cancers but more malignant than the arrhenoblastoma. In 53 adequately studied cases, Döderlein[4] found that 13, or about 25 per cent, had extrapelvic metastases and that 10 of these (18.8 per cent) had died.

It is pre-eminently a tumor of early life, common in children before puberty and in young adolescents, but it may be found at any age. Sex hormone studies give normal results. This bears out the clinical observation that this tumor is of a sexually indifferent type.

Treatment.—While there is no difference of opinion as to the advisability of surgical treatment, there is still some uncertainty as to the extent of the operation in the individual case. Most of the patients are young, so there is a natural tendency to avoid radical operations if possible.

In young patients, with well-encapsulated unilateral tumors, conservative operation appears justified by the good results obtained in many reported cases. This was the course in our case. Where this plan is followed, careful follow-up supervision must be carried out, with radical operation should there be any evidence of recurrence.

Summary

A case of dysgerminoma in an 18-year-old unmarried girl has been presented. After a unilateral salpingo-oophorectomy was performed, the patient had an uneventful recovery. She later married and had a spontaneous delivery of a normal child. A dysgerminoma in the other ovary was discovered about one year after parturition. At this time the remaining ovary and tube together with the uterus were removed.

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RUPTURE OF A FOUR MONTHS GRAVID RUDIMENTARY HORN OF A BICORNATE UTERUS

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A 19-YEAR-OLD woman was referred to the Gynecological Department of the Woman's Hospital, complaining of an excruciating lower abdominal pain followed by fainting and complete exhaustion. She had been married two years prior to admission and aborted a 3 months' fetus without any apparent cause. Forty days after this abortion she became pregnant again, this time without any complication, and delivered a full-term baby with no intervention. Four months previously she became pregnant for the third time and had no complaints until the date of her admission, when she was brought to the hospital in a state of shock.

Fig. 1.—Ruptured gravid uterus bicornis unicollis with one rudimentary horn.

On examination she appeared pale and colorless with cold extremities. Her pulse rate was 140 per minute, thready and almost imperceptible. The rectal temperature was 35° C. and the systolic pressure could hardly be determined at 70.

Abdominal examination showed tenderness in the left lower quadrant. No apparent tumor could be detected. Vaginal examination revealed a soft, closed cervix with slight bloody discharge and extreme sensitivity in the pouch of Douglas. The uterus seemed larger than normal, soft and somewhat irregular, and deviated to the right. The right adnexa were normal, but on the left a tender mass, rather irregular in shape but soft in consistency, could be felt. A diagnosis of ruptured ectopic pregnancy was made and to confirm the diagnosis blood was aspirated from the posterior cul-de-sac.

Since the patient was in shock with a hemoglobin of 50 per cent and red blood count of 2.1 million, it was decided to give her a transfusion on the operating table.

A midline incision was made and on opening the abdomen profuse intra-abdominal hemorrhage with huge blood clots was noticed.

Pelvic exploration showed a bicornate uterus, the rudimentary horn ruptured entirely through the middle. A 4 months' fetus was free in the abdominal cavity and attached by a long cord to the placenta inside the ruptured uterus.

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The right ovary and tube were normal but the left tube seemed very short and rudimentary and the left ovary appeared normal but somewhat misplaced (Figs. 1 and 2).

Since the primary uterus seemed normal in every respect, it was decided to dissect and remove the rudimentary horn from its point of attachment to the uterus near the cervix.

After the fetus was removed and the pelvis was cleansed of blood clots, the abdomen was closed in the usual manner.

The patient received 750 c.c. of blood during the operation and her general condition seemed quite satisfactory at the end of the operation. She was hospitalized for ten days, passed an uneventful course, and was discharged in good condition.

Fig. 2.—Drawing of ruptured rudimentary horn with 4 months' fetus in the abdominal cavity.

Conclusions

1. A case of a 4 months gravid ruptured rudimentary horn in a bicornate uterus unicollis is hereby presented.

2. It is quite logical to deduce that:

a. The first abortion resulted from a pregnancy in the rudimentary horn.

b. The second normal pregnancy and delivery were through the main uterus.

c. The third pregnancy which led to the rupture and escape of the fetus into the abdominal cavity was again in the rudimentary horn, rupture having taken place due to overdistention.

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MASSIVE LEUKEMIC INVASION OF THE INTERNAL FEMALE GENITAL ORGANS IN ACUTE MYELOGENOUS LEUKEMIA

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THE case herein reported appears to be an extremely rare example of acute leukemia causing the formation of a massive tumor in the internal female genital organs. Although it is well known that all types of leukemia can cause soft-tissue tumor formation in all parts of the body, it appears from a review of the literature that this tumorlike infiltration of the internal female genital organs is of infrequent occurrence. Most cases reported to date are examples observed at autopsy rather than clinical or surgical material. Thus Schlagenhaufer,[1] Geipel,[2] and Brakemann[3] observed this invasion of the uterus, tubes, and ovaries at autopsy, Brakemann also reporting infiltration of the vagina. Cases with uterine invasion alone, also as observed at autopsy, have been reported by Strobl,[4] Reiss,[5] Villata,[6] Jürgens,[7] and Poynder,[8] the latter case reported as a chloroma. Further observations of a similar nature are made by Pietro,[9] with involvement of the cervix and right tube, and Thaler,[10] with observation of the infiltration of the tubes only.

The only clinical observation of leukemic infiltration has been reported by Hauptman and Taussig,[11] and Held,[12] who mentioned invasion of the uterus only. McDonald and Waugh[13] also reported leukemic infiltration of the endometrium in uterine curettings. Rusch[14] observed the same in the labium minus, and Kulka[15] in the clitoris.

Case Report

Mrs. R. S., No. 212936, aged 54 years, was admitted to the hospital on April 12, 1954, with the chief complaint of left lower quadrant pain radiating to the left leg, of approximately three weeks' duration. Swelling of the leg, urinary frequency, and dysuria of two days' duration were also noted. Her past history included a subtotal thyroidectomy for thyrotoxicosis in 1943, and rheumatic heart disease with auricular fibrillation and pulmonary infarction in 1950. There followed several admissions in 1952, 1953, and 1954 for cardiac decompensation. She had had nine normal full-term pregnancies, and deliveries. She had been amenorrheic since 1946. No loss of weight had occurred.

Examination revealed a well-developed, well-nourished, white woman, in no apparent distress. Cardiac enlargement to the left was noted. Cardiac rhythm was irregular but no definite murmurs were heard. The entire abdomen was soft and nontender. In the lower abdomen, a nontender, hard, fixed mass was palpated, extending in the midline to 4 cm. above the symphysis pubis. The right leg was normal. The left leg was markedly swollen, hot and tender, with pitting edema throughout. The femoral and the dorsalis pedis pulses were felt bilaterally. No lymphadenopathy was noted in the axillary, inguinal, or femoral regions. Pelvic examination revealed a marked asymmetrical stenosis of the vaginal canal at the junction of the middle and upper thirds, which allowed for the passage of only one finger. Through this constricted area the cervix could be felt, and appeared to be smooth,

fixed, deviated to the right, and attached to the abdominal mass previously described. This mass could also be felt extending laterally to the midportion of the right adnexa, and to the left lateral wall. The mass was extremely hard and irregular.

The temperature was 101° F.; pulse 120 per minute; respirations 28 per minute; and the blood pressure was 130/70 mm. Hg. The complete blood count showed the hemoglobin to be 12 Gm. per 100 c.c.; red blood count 4.4 million; white blood count 14,500. The differential count was: staff cells 14 per cent; neutrophils 39 per cent; lymphocytes 11 per cent; monocytes 8 per cent; myeloblasts 16 per cent; promyelocytes 6 per cent; myelocytes 2 per cent; normoblasts 5 per cent. Urinalysis showed: specific gravity 1.016; albumin 1 to 2 plus; no reduction; microscopic examination negative. The blood chemistry was normal, except for nonprotein nitrogen of 58 mg. per cent, and total proteins of 5.4 Gm. per cent. Papanicolaou smears of the vaginal and cervical secretions were negative for malignancy. X-ray of the chest was essentially negative for lung or medistinal pathology. The cardiac shadow showed generalized enlargement.

Barium enema revealed a well-filled colon with displacement and compression of the distal portion by a soft tissue mass in the pelvis. Intravenous pyelogram showed a mass in the left pelvis, which displaced the bladder to the right, and a nonfunctioning enlarged left kidney.

Cystoscopy demonstrated a markedly distorted bladder with no evidence of a perforating tumor. Repeat electrocardiograms showed auricular flutter. Because of the marked number of immature cell forms noted in the peripheral blood smear, a sternal marrow puncture was performed. This study revealed the following: myeloblasts 85.5 per cent; promyelocytes 0.5 per cent; myelocytes, neutrophils, 0.5 per cent; nonsegmented neutrophils 1.0 per cent; segmented neutrophils 4.0 per cent; lymphocytes 4.5 per cent; monocytes 0.5 per cent; normoblasts 3.5 per cent; the total nucleated cell count was 94,200 per cubic millimeter.

The clinical diagnosis was therefore: (1) cardiac hypertrophy with auricular fibrillation; (2) acute thrombophlebitis of the left lower extremity; (3) acute myelogenous leukemia; and (4) possible pelvic malignancy.

The patient was placed on conservative therapy for the cardiac and leg conditions. Her course showed some general improvement. Repeated vaginal smears were negative for malignancy. It was decided to perform an exploratory laparotomy. On April 24, a complete blood count showed some anemia and an increase in leukocytes to 39,700 per cubic millimeter. The differential count was relatively unchanged.

On April 25, 1954, exploratory laparotomy was performed. The omentum appeared slightly thickened in some areas. The liver was normal with no masses felt. The spleen was enlarged and smooth. Many bowel adhesions were present on the left side of the pelvis which contained a homogeneous, irregular mass filling the entire bony pelvic cavity. It was impossible to differentiate the tube and ovary or to trace the ureter on this side. The mass was very pale and friable, and incorporated in its medial portion was a uterine fundus which was also enlarged, pale, irregular, and friable. The right tube had a similar appearance. It was markedly thickened throughout its entire length, but the fimbriated end could easily be distinguished. The right broad ligament was also thickened and appeared to be involved in the pathological process. On the posterior surface of the broad ligament the right ovary was hanging free, but it was pale, granular, and stony hard. The right ureter could not be located. The process extended down to, and involved, the upper end of the vagina.

It was thought that the entire process represented a localized spread of some malignancy, and therefore a portion of the anterior wall of the uterine fundus and a segment of the right tube were removed for microscopic study. The abdominal contents were then re-explored, but no further neoplasm was encountered. The iliac, hypogastric, and aortic glands were palpated on the right side, but no evidence of enlargement or invasion was noted. The abdomen was then closed.

In spite of a satisfactory postoperative course, the condition of the patient began to deteriorate. Her physical condition on May 1, 1954, became suddenly worse, and she died on May 2, 1954. No autopsy permission was obtained.

Pathological Examination.—The specimens submitted to the pathology department consisted of a portion of the right tube, and a small segment of the anterior wall of the uterus. Tube: Gross examination of the portion of the tube consisted of a thick-walled, edematous, tubular mass, which measured 5.0 by 2.5 by 2.0 cm., and was reddish gray and soft. Microscopic examination: The normal tissues of the tubal wall were completely replaced by large sheets of atypical cells. These cells had a scant cytoplasm, with large hyperchromatic nuclei which showed marked pleomorphism. In the center of the masses of cells, the tubal epithelial structure could be seen (Fig. 1). The biopsy taken from the anterior wall of the uterus revealed an irregular reddish-gray mass which measured 1.5 by 1.0 by 0.5 cm. Microscopic examination showed invasion of atypical cells similar to that noted in the tube.

Both biopsy specimens were interpreted as leukemic infiltration invading the normal pelvic genital organs. However, for the purpose of demonstrating a possible reticulum formation, van Gieson staining was done and was negative.

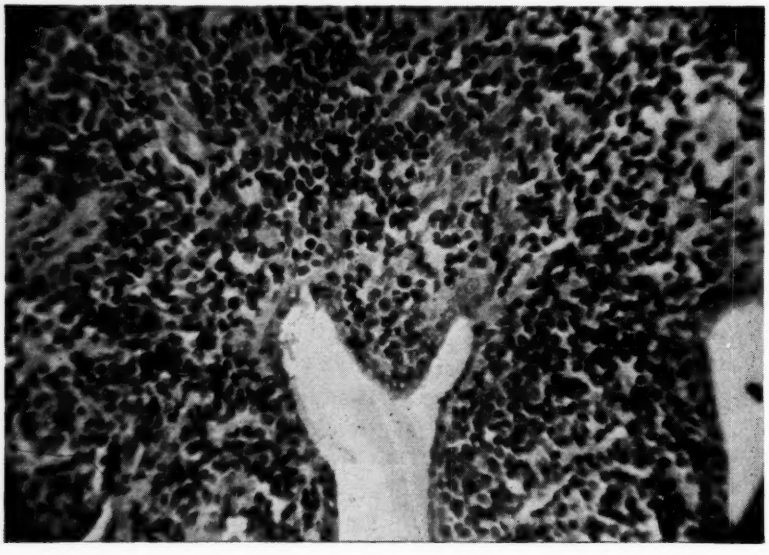

Fig. 1.—Histopathology of Fallopian tube showing the preserved epithelial lining of the tubal lumen and the massive replacement of the tubal wall by the leukemic cells.

Comment

There seems little doubt as to the leukemic nature of the disease. This was well substantiated by the finding of leukemic cells in large numbers in both the peripheral blood and the bone marrow. In addition, this case appears to be the first clinical observation of so massive an infiltration of all the internal female genital organs.

Summary

1. The clinical observation of a rare massive leukemic infiltration of the uterus, tubes, ovaries, parametrium, and vagina is reported.

2. A review of the literature is included and indicates the rarity of this observation.

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A PROCEDURE TO SHORTEN LABOR, AND TO REDUCE THE NEED FOR INTERFERENCE IN OCCIPUT POSTERIOR POSITION AND IN TRANSVERSE ARREST

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AT ONE time the obstetrician feared the posterior position and transverse arrest, thinking that they caused very long labors, and increased morbidity and mortality. Now that fear is dispelled, and one rarely treats such conditions by cesarean section or podalic version and extraction. Our procedure attempts to reduce further the need for interference and to shorten labor in such instances.

In these positions two major factors slow the progress of labor: first, the greater angle of rotation, and, second, the poor flexion of the fetal head. Poor flexion of the fetal head is, however, probably the most frequent factor responsible for variations in rotation.[1] Uterine inertia may develop, and the cervix dilates poorly.

Treatment usually consists of one or more of the following: (1) supportive treatment in the first stage, (2) a pad behind the anterior shoulder held in place by a binder, (3) podalic version and extraction, (4) manual rotation, then forceps, (5) Scanzoni double application of forceps, (6) Kielland forceps, or (7) Barton forceps, (8) manual flexion of the head during a contraction, or (9) delivery in the posterior position.

We propose, in addition to this list, to place the patient in the Trendelenburg position. In addition to abdominal palpation we do a sterile vaginal examination, x-ray, or both. This is to diagnose the position correctly and get a proper evaluation of our procedure.

In normal labor the cervix is retracted upward over the fetal head. With the lengthening of the uterus, the longitudinal fibers are drawn taut, and, since the lower segment and cervix are the only parts of the uterus which will give, these structures are pulled upward over the lower pole of the fetus.[2] In posterior and transverse positions, poor flexion of the fetal head causes a larger diameter to present. If the cervix is not completely dilated, the larger diameter of the fetal head causes greater compression against the cervix and walls of the pelvis. The greater angle of rotation slows labor, and inertia may become evident. This increased pressure over a longer period of time causes edema of the cervix below the point of compression, and caput formation of the fetal head. The edematous cervix does not readily retract over this point of compression.

An analagous situation arises in edema of the anterior lip of the cervix when a patient bears down too soon before complete dilatation. It is caught between the presenting part and the pubic bone. In such instances the patient is placed in the dorsal position with the hips higher than the head. The swollen lip is supported during contractions and pushed upward between pains,[3] when there is the least compression by the presenting part.

In the second stage of labor there is trauma of the soft tissues of the pelvic wall with subsequent edema. Progress is not so greatly delayed since we have one less thickness of tissue to contend with, namely, the cervix.

The object of using the Trendelenburg position is to withdraw the presenting part mechanically from the walls of the pelvis at the point of compression. There is postural drainage and reduction of the edema. With each succeeding contraction the presenting part gets another chance to improve its position.

The following are some of our typical cases briefly outlined:

CASE 1.—Mrs. S. J., No. 39083, aged 42 years, para 0, gravida i, was admitted Feb. 27, 1954. Her last normal menstrual period was May 16, 1953. The estimated date of confinement was Feb. 21, 1954. She was admitted for induction because she was an elderly primigravida, postmature, with a large baby. X-ray upon admission showed the fetus to be in the left occipitoposterior position, the measurements adequate, and the pelvis gynecoid. One-half minim Pitocin was given subcutaneously at 5:26 P.M., 6:00 P.M., 7:30 P.M., and 8:30 P.M. A sterile vaginal examination at 6:00 P.M. showed the cervix to be 1 cm. dilated. The membranes were artificially ruptured. At 8:00 P.M. she was having irregular pains, and the cervix was 2 cm. dilated. At 8:45 P.M. the pains were regular and strong. She was given Demerol, 50 mg., and scopolamine, $\frac{1}{200}$ grain. The 50 mg. Demerol was repeated at 10:15 P.M. and at 12:30 A.M. At 11:30 P.M. the cervix was still 2 cm. dilated. The patient was placed in the Trendelenburg position. At 12:35 A.M. the cervix was 5 cm. dilated, and at 2:15 A.M. dilatation was complete. She was delivered of an 8 pound 8½ ounce female infant by prophylactic low forceps and right mediolateral episiotomy from the left occipitoanterior position under cyclopropane anesthesia. The placenta was expressed at 3:50 A.M.

CASE 2.—Mrs. T. J. G., No. 34136, admitted Dec. 5, 1953, aged 27 years, para i, gravida ii, had her last normal menstrual period on March 13, 1953. The estimated date of confinement was Dec. 20, 1953. Labor started spontaneously at noon the day of admission. The membranes were artificially ruptured at 5:10 P.M. during a sterile vaginal examination. The cervix was 5 cm. dilated. The position was left occipitoposterior. At 5:40 P.M. the pains were strong. Rectal examination showed the cervix to be 6 cm. dilated. She was given Demerol, 100 mg., and scopolamine, $\frac{1}{150}$ grain at 5:45 P.M. At 6:30 P.M. the patient was complaining and her contractions were strong. The cervix was still 6 cm. dilated, so she was placed in the Trendelenburg position. At 7:00 P.M. the cervix was completely dilated, and the head was on the perineum. At 7:11 P.M. the patient was delivered of a 7 pound 6½ ounce female infant from the left occipitoanterior position, spontaneously, after a right mediolateral episiotomy, with cyclopropane anesthesia. The placenta was expressed at 7:16 P.M.

CASE 3.—Mrs. M. R. K., No. 45952, aged 21 years, para 0, gravida i, was admitted June 17, 1954. The last menstrual period was Sept. 21, 1953, and the estimated date of confinement June 28, 1954. She was admitted for elective induction after x-ray on June 15, 1954, had shown the position to be right occipitotransverse. This was the finding upon admission and during labor. The pelvis was gynecoid in type and measurements were adequate. Intravenous Pitocin, 15 minims to 1,000 c.c. 5 per cent glucose in distilled water, was started at 9:53 A.M. Seconal, 1½ grains, was given at 10:10 A.M. and 11:10 A.M. At 10:30 A.M. the cervix was 2 cm. dilated. At 2:15 P.M. a sterile vaginal examination was done and the membranes were artificially ruptured. The cervix was 3 cm. dilated. At 3:10 P.M. Demerol, 100 mg., and scopolamine, $\frac{1}{150}$ grain, were given intramuscularly. At 6:15 P.M. the cervix was

7 cm. dilated At 6:30 P.M. she was given Demerol, 75 mg. At 9:00 P.M. a sterile vaginal examination showed the position still to be occipitotransverse and the cervix still 7 cm. dilated. At 9:30 P.M. she was placed in the Trendelenburg position. At 10:05 P.M. the cervix was completely dilated and the head was upon the perineum. At 10:22 P.M. she was delivered of a 6 pound 12½ ounce male infant by prophylactic low forceps and right mediolateral episiotomy under cyclopropane anesthesia.

CASE 4.—Mrs. M. N., No. 45720, was admitted June 13, 1954. She was 23 years old, para ii, gravida iii, with the last menstrual period Aug. 29, 1953, and the estimated date of confinement June 5, 1954. Labor began spontaneously at noon the day of admission. At 7:50 P.M. the contractions were every 7 minutes. Rectal examination showed the vertex at station minus 3 and the cervix 1.5 cm. dilated. At 11:15 P.M. she was given Seconal, 3 grains orally. At 1:00 P.M. the following day she was complaining of a backache and was given Seconal, 1½ grains orally. At 2:55 P.M. a sterile vaginal examination was done and the membranes were artificially ruptured. The cervix was 5 cm. dilated, the vertex was at station 0 and in the right occipitoposterior position. At 3:00 P.M. Demerol, 100 mg., and atropine, 1/150 grain, were given intramuscularly. The patient was placed in the Trendelenburg position. At 3:30 P.M. the cervix was completely dilated and the presenting part was in the right occipitoanterior position. She was given a saddle block anesthetic. At 3:40 P.M. she was delivered of a 6 pound 13 ounce male infant by prophylactic low forceps and midline episiotomy.

We have tried this procedure on apparently normal patients with known posterior and transverse positions in cases where there was a delay in the progress of labor. We are cognizant of the fact that many babies rotate spontaneously without delay from the posterior and transverse positions. We avoid the procedure in medically complicated cases.

This small series of twenty-four cases represents a preliminary report, and we are continuing this study.

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A TYPHOID ULCER OF THE EXTERNAL GENITALS

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THE presence of genital ulcers in association with typhoid fever is a rare phenomenon. Today's standard medical texts do not even mention such lesions. The literature of a half century ago does, however, contain a few references which indicate that genital lesions do occur in typhoid, but are rare. Keen[1] in 1898 located 17 cases of typhoid lesions of the vulva and vagina. They appeared as single, occasionally as multiple, ulcers which varied in size from a few millimeters to a few centimeters in diameter. The ulcers were described as being very painful, and their bases were covered with a purulent exudate. Edema distorted the surrounding perineum. The age distribution was primarily between 17 and 27, and he described the disorder as manifesting itself "by either a distinct gangrene of the external genitalia or by gangrenous ulcers of the vagina." Some of Keen's cases were so severe that the lesions progressed to rectovaginal fistulas and stenosis of the vagina. Lartigau,[2] one year later, added 2 cases of multiple ulcers of the external genitals from which he cultured typhoid bacilli.

Case Report

On Aug. 14, 1953, a 12-year-old girl was admitted to the hospital with an unexplained fever of 5 days' duration, ranging from 104 to 106° F. Her illness began on August 9 with a bifrontal headache, malaise, and feverishness. Within a few hours she developed a sore throat and meningismus. Her temperature rose to 104° F. and although examination did not reveal any specific diagnostic signs, it was thought expedient to begin penicillin and sulfadiazine therapy. The patient's status did not change on the drugs, and the following day, coincidentally with the onset of explosive diarrhea, she noted 3 to 4 small vulval ulcerations and increasing edema of the vulva. Aureomycin was added orally, and local penicillin was applied to the vulva. This regimen was maintained for four days, but the temperature did not fall. A gynecologist was called in the hope that he might identify the vaginal lesions. Examination of the genitals the day before admission, which was the fourth day of the illness, disclosed a large 2 cm. ulcer on the medial aspect of a markedly edematous left labium minus (Fig. 1). The edges of the lesion were raised and its base was grayish and covered with necrotic tissue and feces. A few 2 to 3 mm. satellite lesions surrounded the ulcer. The external genitals were exquisitely tender. It was thought that the ulcers were secondary to the fever, or perhaps caused by a viral infection. Buccal ulcers were not present. Local cleansing with pHisoHex and benzalkonium chloride was ordered. The blood count was normal and the sedimentation rate was elevated slightly. In spite of the previously mentioned antibiotics and supportive therapy, the patient failed to improve and therefore was taken to The New York Hospital. The blood culture taken

on August 14, the day of admission, was reported on August 17 as positive for *Salmonella typhosa*. Chloramphenicol therapy was begun. The patient responded excellently to this and in three days was afebrile. The labial lesions and edema began to disappear almost immediately and on August 25, eight days after chloramphenicol was started, the genitals were normal. Unfortunately, many fecal cultures were overgrown with *Proteus vulgaris*, and it was not until the eighteenth day of the illness that *Salmonella typhosa* were obtained from the feces. No cultures were taken from the ulcer because it was grossly contaminated by feces and urine. At re-examination eleven months after discharge, there were no residua except for minimal retraction and scar tissue in the area of the ulcer.

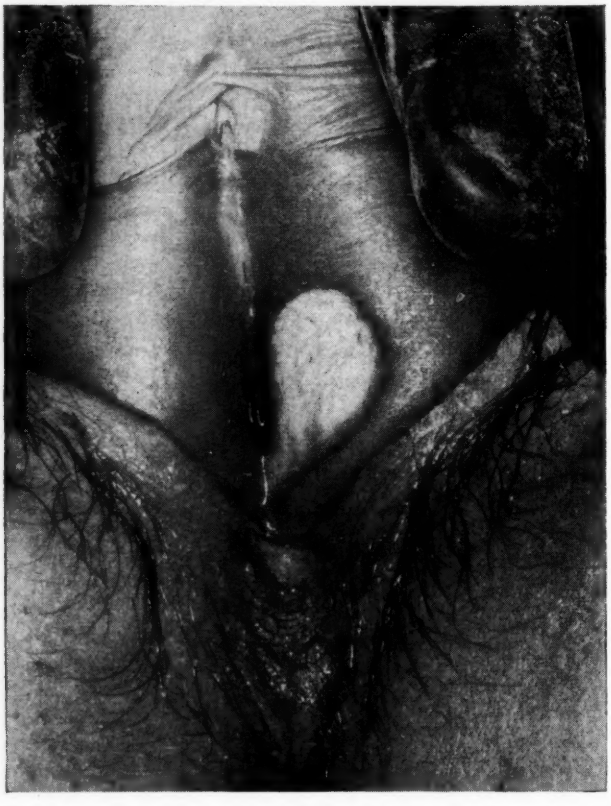

Fig. 1.—A 2 cm. typhoid ulcer of the left labium minus. Note marked edema of the labia minora.

The pathogenesis of the ulceration remains a matter of speculation. It is possible that the ulceration is a result of bacterial emboli to an area which is moist and liable to macerate easily. Some[2] have considered the lesions secondary to direct inoculation by feces and urine. Kehrer[3] was undecided concerning the origin of the ulcers and considered them secondary to a high fever, and due to a combination of bacteria. He said the positive cultures for *Salmonella typhosa* were from the contaminating urine and feces. No definite conclusion can be reached. In years gone by the lesions healed when the patient recovered, and in the reported case only after the institution of chloramphenicol therapy.

Summary

An ulcer of the external genitals in association with typhoid fever has been presented. Although biopsies and cultures were not taken because of gross fecal and urine contamination, the ulcer is believed to be typhoid in origin. The lesion appeared while the blood stream was invaded with *Salmonella typhosa* and regressed only after chloramphenicol therapy was begun.

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MALIGNANT TERATOMA OF THE OVARY, PRIMARY CHORIONEPITHELIOMA, AND SARCOMA

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AN OVARIAN tumor in which chorionepithelioma and sarcoma are also found is an extreme rarity. A malignant teratoma of the ovary represents one of Nature's earliest and most malignant transformations. Neither the historical advances in the recognition and understanding of embryological pathology nor the various theories to account for the development of a teratomatous chorionepithelioma will be presented. Forty years ago, Ewing wrote: "In 1895, Marchand demonstrated that the decidual sarcoma of Sanger was derived from chorionic epithelium and named this tumor 'chorioepithelioma.' It was felt that the many difficulties encountered in diagnosis and treatment would be eliminated. . . . It may be justly said that the study of chorioepithelioma presents more peculiar problems and its diagnosis, prognosis and treatment encounter more special difficulties than exist with any other known tumor process." This statement is as true today as when it was written. True primary chorionepithelioma of the ovary is an exceedingly rare tumor, the exact number in the literature being difficult to establish. However, no case of a primary chorionepithelioma of the ovary associated with a sarcoma, myxoma, myxosarcoma, chondroma, and cystadenoma could be found.

Case Report

The patient was a 14-year-old white girl admitted to the Greenpoint Hospital, Brooklyn, New York, Oct. 2, 1949, complaining of increasing abdominal girth, weakness, and dyspnea of several weeks' duration. Menses began at 12, occurring every twenty-eight days, lasting five days. The last menstrual period started when expected, on September 28, but consisted of spotting for four days with no actual menstrual flow. Coitus was denied. Childhood diseases included measles, mumps, and chicken pox but no serious illness. Three weeks prior to admission, the patient began to notice dyspnea on exertion, as well as generalized weakness. The remainder of the history was noncontributory.

Physical examination showed a sallow, pale young girl of 14 in the semi-orthopneic position in no acute distress. Positive findings in the chest revealed dullness to flatness bilaterally in the posterior chest from the sixth interspace down; edema of the paravertebral area. The abdomen was tense, tender, and enlarged. An irregular nodular mass approximately 25 to 30 cm. by 25 cm. was felt arising from the pelvis but was difficult to outline. A vaginal examination was omitted as the patient had a virginal introitus with a very small hymenal opening. Rectal examination disclosed a small cervix pointing to the left and posteriorly; an anterior small mobile uterus with the parametria soft, not thickened, and not tender. The adnexa could not be felt. The cul-de-sac was free. The blood pressure was 112/68, temperature 101.2° F., pulse 120. Laboratory findings showed hemoglobin 10.5 Gm., erythrocyte count 3.5 million; leukocyte count 14,000 with a normal differential

count. The sedimentation rate was 16 mm. in one hour. The urine was normal. Wassermann and Mazzini tests were negative. Acid and alkaline phosphatase was normal. Blood chemistry showed: total proteins 5.5: albumin 3.40, globulin 2.11 Gm. per cent; urea nitrogen 15 mg. per cent; sugar 86 mg. per cent; uric acid nitrogen 4.0 mg. per cent. X-ray of the abdomen revealed a homogeneous mass filling most of the abdominal cavity; both domes of the diaphragm were elevated. A chest plate showed a small area in the right upper lobe between the first and second rib suggestive of a healed Koch infection. The preoperative diagnosis was pseudomucinous cystadenocarcinoma.

Fig. 1.

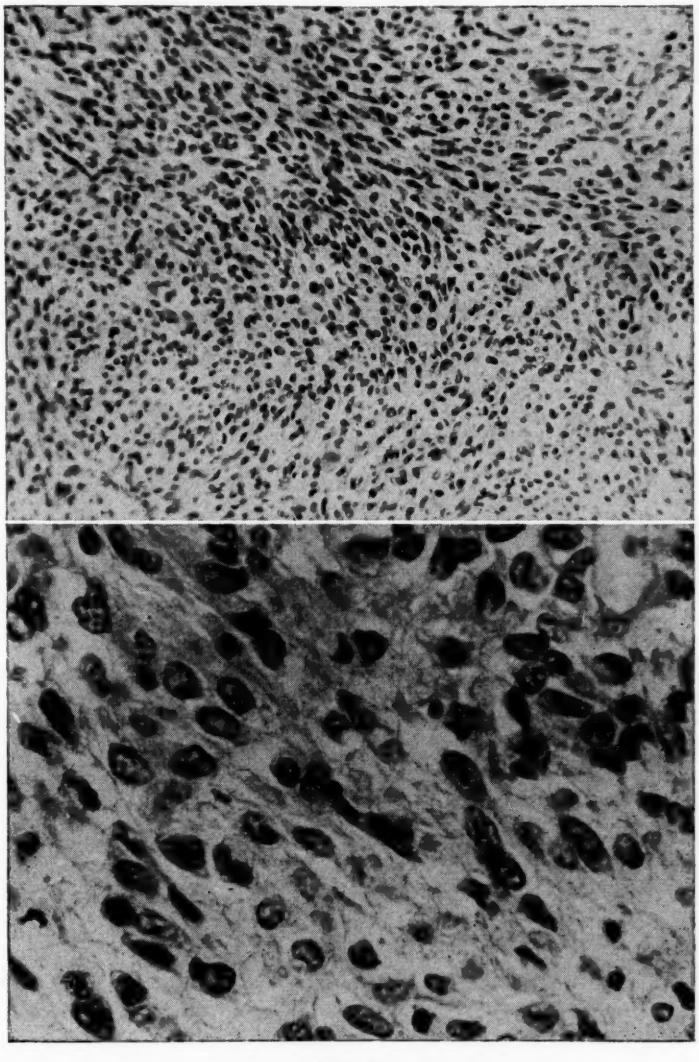

Fig. 2.

Fig. 1.—Area of spindle-cell sarcoma. (×300; reduced ⅓.)
Fig. 2.—High power of sarcomatous area. (×600; reduced ⅓.)

The patient was operated upon on Oct. 7, 1949. Clear greenish-yellow slightly viscid fluid was found in the abdomen associated with a myxomatous velamentous mass some 30 cm. in diameter arising from the pelvis, specifically the right ovary. Solid and cystic papillary areas were noted in the tumor as well as several areas of recent hemorrhage. The

tumor was attached to the anterior, lateral, and posterior peritoneal wall, omentum, and bowel. Infiltration and attachment of the tumor to the broad ligament and infundibulopelvic ligament were noted. A supravaginal hysterectomy and bilateral salpingo-oophorectomy were performed with the removal of as much of the neoplasm as was possible.

The patient made an uneventful postoperative recovery and was discharged on the tenth postoperative day. She was admitted to the Kings County Hospital, Brooklyn, New York, on Nov. 2, 1949, because of abdominal pain, anorexia, weakness, and a nonproductive cough. X-ray examination of the chest revealed bilateral pulmonary metastases. Her general condition declined rapidly and she died on Nov. 19, 1949.

Fig. 3.—Myxomatous change from segment of tumor with extravasated red blood cells and leukocytes. (×300; reduced ⅕.)

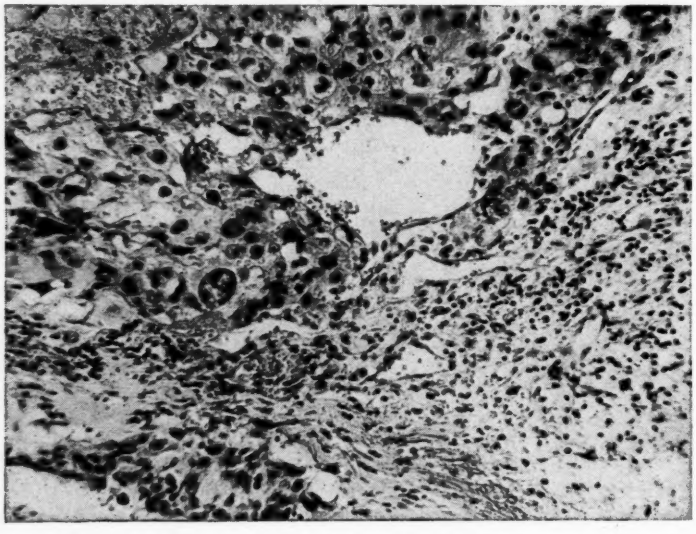

Fig. 4.—Area of chorionepithelioma with adjacent hemorrhage and leukocytic infiltration. (×300; redueed ⅕.)

Pathological Report.—The uterus, removed supracervically, measured 5 by 5 by 3 cm., with a smooth, glistening serosa except for the right fundal area where the serosa was rough-

ened with grayish-white fibrous tags. On cut section, the myometrium was firm, grayish white, and measured 1 cm. in thickness. No significant changes were noted in the myometrium or endometrium. The left tube and ovary appeared grossly normal.

The tumor mass appeared to arise from the right ovary, completely destroying its gross appearance. The right tube was intimately attached to the mass, . . . tube and ovary measured 30 by 26 by 15 cm. The external surface of the neoplasm was somewhat firm, lobulated, and partially cystic, presenting numerous translucent cysts varying in size from several millimeters up to 5 to 6 cm. A number of the cysts showed hemorrhagic areas, recent and old. Here and there small irregularly oval spaces were encountered containing colorless viscid fluid. Separating the nodular areas were zones of firm, dense, trabeculated grayish tissue interspersed with numerous small, translucent fields. The previously mentioned cystic areas noted on the external surface presented thin-walled cavities filled with colorless or reddish, gelatinous material. Toward one pole, the tumor presented a mass of lobulated, soft, gelatinous ovarian tissue yielding a large amount of mucoid material. No characteristic ovarian tissue was identified grossly.

The microscopic slides showed a normal endometrium in the proliferative phase. The right ovary revealed an unusual picture of a malignant teratoma, showing a primary chorionepithelioma as well as areas of sarcoma and myxosarcoma. Other areas of the tumor showed chondromatous tissue as well as a small papillary cystadenoma. Throughout areas of the tumor, hemorrhage and necrosis in association with the chorionepithelioma were evident. Figs. 1 through 4 show the salient microscopic appearance of the tumor elements.

Autopsy Report.—The body was that of a 14-year-old girl, admitted to the Kings County Hospital Nov. 2, 1949, who died Nov. 19, 1949. The postmortem was held Nov. 20, 1949. The mammary glands were of the usual female type without evidence of colostrum. Upon opening the peritoneal cavity, all organs within the cavity were found obscured by a tremendous myxomatous, glairy, sticky tumor which apparently had also infiltrated the abdominal peritoneum and musculature. The omentum could not be identified per se. The stomach and entire gastrointestinal tract were seen completely covered by the tumor mass. The pelvic organs were not identifiable because of the extensive tumor growth.

No free blood or fluid was found in the thoracic cavity. Both lungs presented a cherry-red color with multiple metastatic tumor nodules present on both sides. Each lung weighed 350 grams. They were reddish in appearance and showed multiple metastatic nodules throughout all lobes. On cut section, the nodules were round, circumscribed, hard, gray white in appearance; some showed central necrosis and hemorrhage. The lung parenchyma showed minimal edema but no evidence of infiltration.

The liver had a smooth and glistening capsule with part of the tumor mass adherent to the lower border of the right lobe.

The kidneys did not show any gross abnormalities.

The tumor tissue was of a semisolid friable consistency with tremendous amounts of myxomatous material covering the tumor mass. The tumor had spread like a grapevine to involve and envelop every space, crevice, and organ throughout the entire abdominal cavity.

The microscopic picture of the autopsy material did not deviate from the original description of the tumor. The lungs contained multiple metastatic nodules which showed the typical picture of chorionepithelioma and no other tumor element.

Summary

A case report is presented of a 14-year-old white virginal female with a malignant teratoma in which a primary chorionepithelioma, sarcoma, myxosarcoma, myxoma, chondroma, and a papillary cystadenoma were found. The gross and microscopic appearance of the tumor, as well as the autopsy report, were described.

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PREGNANCY AND LABOR COMPLICATED BY PELVIC ECTOPIC KIDNEY ANOMALY AND UTERINE ANOMALY

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AS FAR as we can find in the literature, this is the first case reported of bilateral renal pelvic ectopia with fusion associated with a uterus arcuatus. Three cases of bilateral ectopia with fusion have been reported[1] but they were not associated with uterine abnormalities.

Case Report

Mrs. J. M. E., aged 32 years, gravida iii, para i, was first seen in our office on May 5, 1953. Her last menstrual period was March 12, 1953, with term on Dec. 18, 1953.

Past History.—Her first pregnancy had terminated by spontaneous abortion at eight weeks' gestation in 1941. The second pregnancy had a very smooth and normal course, and was terminated by full-term delivery in 1944. This was a difficult breech extraction made possible by Dührssen's incisions of the cervix after a long labor. The child weighed 5 pounds, 10 ounces, and recovered normally. The patient was very ill afterward with a severe kidney infection. During treatment for this severe postpartum pyelitis or pyelonephritis, pyelograms were made, revealing, for the first time, renal pelvic ectopia of both kidneys. Both kidneys were in the true pelvis below the pelvic brim and overlying the sacrum. The ureters were found to be only 1 to 2 inches in length. For almost three years after the delivery, the patient had numerous hospital admissions for kidney disease; and until we first saw her, she had had constant pyuria and positive kidney cultures. This pyuria was kept under control but not cured by constant supervision of a urologist.

The past history showed that the menses had begun at the age of 13 with 28 day intervals, and 3 to 5 days of flow. The patient had never had molar dentition; there was absence of lactation after her full-term delivery; and no change in the breasts had occurred during pregnancy.

Present Illness.—The patient complained of having missed two periods and of feeling very bad generally. The frog test two and one-half weeks previously was found to be negative. No nausea, emesis, breast fullness, frequency of urination, or constipation had occurred.

Physical Examination.—She appeared to be a well-nourished and well-developed white woman, 5 feet ½ inch tall, who weighed 119 pounds. The teeth showed no molar dentition.

Pelvic Examination.—There was good pelvic support with a shallow vagina. The cervix was fixed and the posterior lip was adherent to the posterior left fornix. An old cervical laceration was present at this site. The cervix was also slightly softened. The uterus was anterior, and a deviation could be felt to the left and to the right, giving the impression of a bicornate or malformed uterus, or else a uterus in which there was a tumor, or perhaps a large ovary adherent to the right side of the uterus. The left portion of the uterus was softened and enlarged to the size of an eight weeks' gestation. The right portion was very hard. The adnexa were negative.

Laboratory Tests.—The erythrocyte count was 4.6 million, the leukocyte count 10,300 with 70 per cent segmented forms, the Kahn test negative, Rh_0, negative, and Friedman test positive. A catheterized urine specimen showed some clumps of pus cells.

Initial Diagnosis.—

1. A pregnancy of eight weeks in the left side of a malformed uterus.
2. Previous dystocia followed by a difficult operative delivery.

3. Bilateral pelvic renal ectopia with chronic pyuria.
4. Old lacerations of the cervix with adherence of cervix to vagina.
5. Rh_0 negative.
6. Other congenital abnormalities as absence of molar dentition and lactation.
7. Possible uterine tumor or cystic ovary adherent to the uterus.

Consultation with the patient's urologist confirmed our belief that the pregnancy should continue; but that instead of delivery from below, elective cesarean section followed by postpartum sterilization should be done; and if gross uterine abnormality was found, hysterectomy should be done at the time of cesarean section rather than sterilization.

Prenatal Course.—The patient's prenatal course was essentially uneventful. The pyuria, present at the initial examination, readily responded to Gantrisin therapy and remained quiescent until after delivery. At twenty-three weeks' gestation, she developed bronchitis which responded to penicillin therapy. At thirty-three weeks' gestation, the patient began to complain of severe pain over the gall bladder region referred through to the back. Physical examination was negative except that the uterine malformation was more noticeable, the fetus lying in a transverse position with the head on the right and pressing over the region of the gall bladder. She was given a gall bladder diet, magnesium sulfate, nitroglycerin, Ketochol, and sedative. No relief was obtained. The pain became so severe at thirty-six weeks' gestation that hospitalization was necessary.

Hospital Course.—On admission on Nov. 9, 1953, heavy sedation, parenteral fluids, atropine, Combiotic, and other supportive measures were given. The gall bladder pain continued to be so severe as to necessitate large doses of narcotics. X-ray examination of the gall bladder was begun on the morning of Nov. 12, 1953. Just before going to the x-ray department, the patient began having regular, painful uterine contractions. The transverse position of the fetus was still present and the fetal heart tones were normal.

X-Ray Report.—A kidney, ureter, and bladder film and spot film over the gall bladder region showed good concentration of the contrast medium within the gall bladder. There was no evidence of intraluminal stone shadows. The dependent portion of the gall bladder was pushed upward by the fetal head. There was a single fetus in transverse position, with marked hyperextension of the head on the trunk. The uterus was of the bicornate variety with the fetal head in the most superior portion of the right horn of the uterus. The fetus appeared to be of approximately seven and one-half months' gestation.

The findings of extreme pain which could not be relieved, malposition of the fetus with severe extension of the fetal head, and onset of premature labor led us to the conclusion that immediate termination of the pregnancy was necessary.

A spinal anesthetic was given. Classical cesarean section was done without difficulty. A normal living female infant, weighing 5 pounds, 4 ounces, delivered by double footling extraction, cried strongly and immediately. After the uterus contracted, it was found to be of the arcuate type rather than bicornate. Subtotal hysterectomy was then done without difficulty. Complete abdominal exploration showed, in addition to the malformed uterus, that the kidneys were of the fused horseshoe type, were lying in the true pelvis below the sacral promontory, and were fused across the midline. These kidneys completely filled the true pelvis. We were amazed how it was at all possible for the previous delivery to have been from below, as the birth canal was so completely obstructed by the kidneys. The tubes, ovaries, and other abdominal organs appeared normal.

Pathological Report.—Microscopic diagnosis: (1) uterus arcuatus; (2) postpartum uterus.

Postoperative Course.—The postoperative course was essentially uneventful. The highest temperature was 99.2° F. on the first postoperative day. A mild cystitis was easily controlled by Thiosulfil. The patient and baby were discharged home on the seventh postoperative day. Follow-up until the present date, July 1, 1954, shows a mother and child in perfect health.

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MESONEPHRIC-DUCT ADENOCARCINOMA

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GARTNER'S duct may persist in the adult woman as a distal remnant of the Wolffian or mesonephric duct. The duct may extend as a continuation of the longitudinal duct of the epoophoron along the oviduct and the uterus, lodged between the peritoneal layers of the broad ligaments. It leaves the uterus at the cervicovaginal junction and descends in the lateral wall of the vagina, close to the hymen. The course of the duct, however, is extremely varied in both the uterus and the vaginal wall.[1]

The mesonephric duct persisted in 20 per cent of the fetuses Meyer[2] examined, and remnants of mesonephric origin in the adult cervix are found in at least 1 per cent of all routine cervical sections.[3] Huffman,[4] however, studied 1,192 surgically excised cervices and found evidence of mesonephric remnants in only 10 of his specimens.

Three types of neoplastic changes are known to occur from mesonephric remnants in the cervix, these being adenomatous proliferations, cysts, and adenocarcinomas. Adenomatous proliferations were described first in 1897 and the adenocarcinoma type in 1903 by Meyer. Henkel[5] reported cystic changes in 1920.

The only references to this subject in the American literature are the papers of Wolfe's[1] in 1940, that of Huffman's in 1948, and Nace's[6] in 1952. Curtis states, however, that one adenocarcinoma arising from a mesonephric remnant in the cervix has been studied at the Northwestern University Gynecological Laboratory and Dr. K. G. Ober of Marburg, Germany, had sent him sections and photographs of a similar case.

Adenocarcinoma of the mesonephric duct remnants in the cervix is usually found in the anterolateral or posterolateral midcervical wall and grossly appears as a gray-white or reddish friable material as differentiated from the remainder of the cervix. Microscopically, the growth consists almost entirely of tightly packed tubules. These tubules are of various sizes and present an unorganized arrangement. Lumina are distended or narrowed, and epithelial proliferations project into the tubular lumina in some areas. The cells lining the tubules are irregular in height and contain large oval or round nuclei, lightly staining, and a large number of mitoses.

Eight cases of adenocarcinoma of the mesonephric duct now appear in the literature, and the following case is the ninth to be reported.

Case History

Miss A. S. (No. Y-4718), white, aged 27 years, gravida 0, was admitted to St. Luke's Hospital, Oct. 11, 1951, complaining of irregular menses for the past year. Periods had been occurring every fourteen days with the flow lasting seven to fourteen days. Previously, the periods were regular every twenty-eight days and lasted for seven days. Systemic review showed only that the patient had been treated for idiopathic epilepsy since the age of 12 with Dilantin sodium and phenobarbital. Vaginal examination showed a nulliparous introitus.

There was a grayish cauliflower-like growth appearing to originate from and involving the entire cervix to such an extent that the external os could not be identified. The growth measured approximately 2.5 by 2 by 2 cm. Extension was not present and the growth was limited to the cervix. The body of the uterus was of normal size. The tubes and ovaries presented no apparent abnormality. Operation on October 16 consisted of biopsy and cauterization of the cervix. Microscopically, multiple sections presented areas of sheets, strands and clumps of cells in a disorderly arrangement. Some sections showed a bizarre glandular pattern which resembled the usual endocervical arrangement. Here the cells were polygonal, cuboidal, or columnar, had vacuolated cystoplasm and intensely hyperchromatic nuclei. Everywhere there was an abundance of atypical mitoses with numerous giant forms and much evidence of stromal invasion.

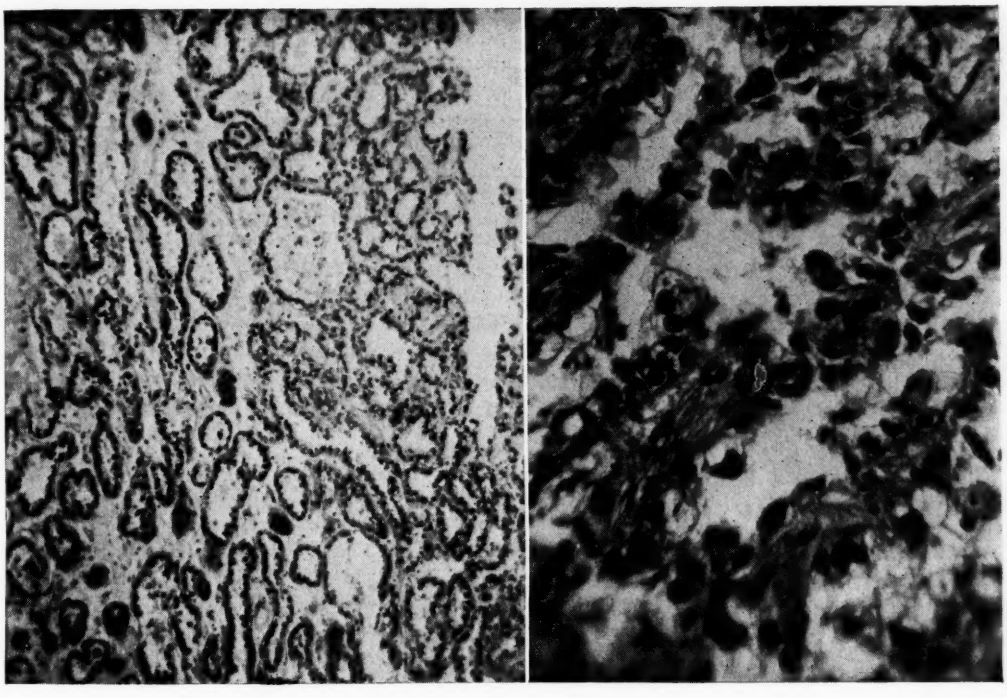

Fig. 1. Fig. 2.

Fig. 1.—Photomicrograph of adenocarcinoma of mesonephric origin in the cervix showing numerous often closely packed tubules. These tubules are disorganized and vary in size.

Fig. 2.—High-power view of the constituent cells of the tubules showing an irregularity in the height of the cells and the position of the nuclei, which contain an increased number of mitoses.

The pathologist felt that the sections presented features of sarcoma botryoides, but some areas were suggestive of adenocarcinoma of the cervix. The slides were sent to Dr. Emil Novak for his opinion.

Novak upon personal communication is quoted: "On the assumption that there is no neoplasm in the ovary, I would interpret your sections as representing a tumor of mesonephric origin, arising from the vestiges of the Gartner duct, which are often found in the lateral vaginal fornices and deep in the substance of the cervix. I have seen a number of cervical adenocarcinomas arising from these elements. Both the clear-cell carcinoma of the ovary and the mesonephroma are believed to be of mesonephric origin, and in a number of ovarian tumors, I have seen exactly the same association which is shown in your tumor."

Diagnosis.—Anaplastic glandular carcinoma.

Following the pathological diagnosis, operation on Oct. 18, 1951, consisted of dilatation and curettage, this time no difficulty being encountered in localizing the external os. Radium was applied in a dose of 100 mg. intra- and contracervically for a total of 5,000 mg. hr. Upon removal of the radium, the patient was discharged and six weeks later was readmitted to the hospital at which time a total hysterectomy, double salpingo-oophorectomy, and incidental appendectomy were performed. At laparotomy, the uterus was slightly enlarged and freely movable. Both tubes and ovaries were normal. The carcinoma had infiltrated into the left paracervical region. As much of the extension as possible was removed. The patient withstood the operative procedure well and, following an uneventful course, was discharged on the fourteenth postoperative day. Follow-up therapy consisted of x-ray radiation; a total of 3,900 r was administered to six fields.

When seen three weeks postoperatively, the patient was free from subjective complaints. The abdominal incision was healed well and the vault of the vagina was healed. On May 11, 1953, the patient was symptom free and had no vaginal discharge. The walls of the vagina were soft and no nodular areas were palpable. In January, 1954, the patient remained symptom free, the walls of the vagina were soft, and induration was absent.

Summary

A case of adenocarcinoma has been reported. The symptoms, physical findings, and microscopic pathology are described.

A number of cases of adenocarcinomas of the mesonephric duct have been reported since Meyer's first description of the tumor in 1903.

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THE TRACHELOTOME, A NEW INSTRUMENT FOR CONING THE CERVIX

FRANK C. SPENCER, M.D., HONOLULU, T.H.

THE vaginal smear method was first introduced by Papanicolaou and Traut in 1943. Since then the literature has become voluminous reporting the widespread application of this method. To obtain an adequate biopsy in cases where suspicious or positive smears have been reported and no visible lesion is present has excited the interest of many and instruments have been devised to obtain such biopsy material. Still another instrument is presented for that purpose.

This coning instrument consists of a cone, blade, tip, and handle. The instrument is assembled by placing the blade on the cone, inserting the handle through the cone and screwing the handle into the tip. The blade is thus securely locked on the cone.

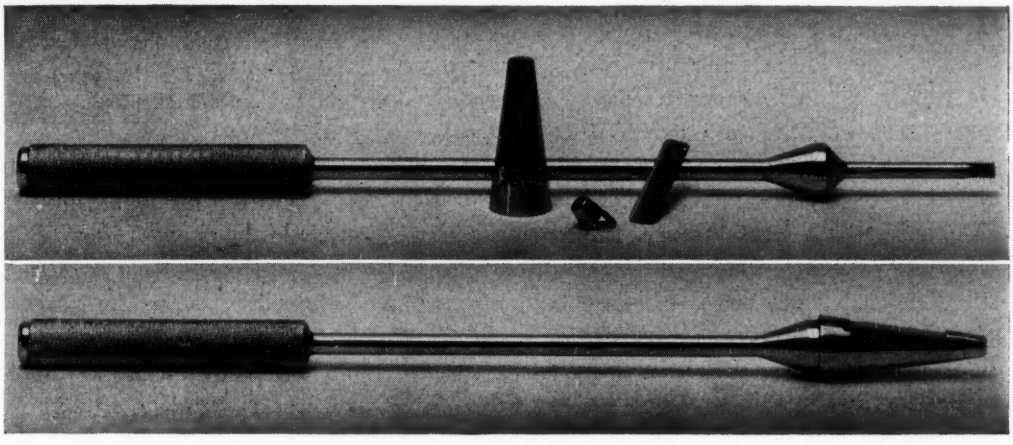

Fig. 1.

The technique of using the instrument is as follows: The cervix must be dilated to at least a size 20 French sound to allow proper introduction and manipulation of the instrument. After the cervix has been dilated the anterior and posterior lips are each grasped with a single-tooth tenaculum to stabilize the cervix while the instrument is being used. The instrument is then introduced and, starting at twelve o'clock, with short cutting strokes, the cervix is completely circumscribed. One of the sulfonamide powders is then dusted or sprayed against the cervix and the vagina is *firmly* packed with dry gauze. This packing is left in situ for forty-eight hours when it is removed and the vagina again firmly packed with dry gauze. A third packing is seldom necessary.

The biopsied tissue is found in the cone and if the instrument has been maneuvered correctly will be found in one sheet ½ to ¾ inch wide, 1 inch long, and about 1/16 inch in thickness. If the squamous edge is then streaked with mercurochrome and the tissue is spread out on a blotter before it is placed in formalin solution it will not curl and the pathologist is better oriented.

This instrument has the following advantages:

1. There is an adjustable and disposable blade (Schick razor).
2. It removes the entire squamocolumnar junction in one sheet of tissue.
3. It cuts deep enough to show if any lesion is invasive.
4. There is no troublesome bleeding requiring sutures.
5. Bleeding is controlled by *firm* vaginal packing.
6. There is no secondary hemorrhage.
7. It may be used as an office procedure.

A REPORT OF A FATAL HEMORRHAGE DUE TO PEPTIC ULCER IN PREGNANCY

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THERE have been 17 deaths due to perforation or hemorrhage from peptic ulcer during pregnancy or the puerperium reported in the literature. Sandweiss[12] reviewed the literature to 1943 and found 13 cases confirmed by autopsy. He reported the fourteenth case. Anderson[1] reported the fifteenth and Johnston[7] reviewed the literature to 1953 and reported 2 additional cases.

Some interesting statistics concerning the 17 cases are: (1) 10 had duodenal ulcers, 7 had gastric ulcers; (2) 12 died of perforation, 5 died of hemorrhage; (3) there was a past history of gastrointestinal symptoms in 6 cases; (4) the diagnosis of peptic ulcer was entertained in only 3 cases.

Pregnancy has always been considered to have a beneficial effect on peptic ulcer,[3, 11] although there is some evidence which supports the theory that toxemia of pregnancy and peptic ulcer have a related etiological basis, which is placental adrenocorticotropic hormone.[2]

Sandweiss[11] reported on 52 pregnancies which occurred in 25 women who had peptic ulcers and, in all but one, the symptoms referable to the ulcer disappeared. Further proof that pregnancy is beneficial to ulcer patients is the rare occurrence of ulcer during pregnancy. Sandweiss[12] reported one death due to perforation of a duodenal ulcer occurring at six months' gestation in 70,310 pregnancies. Hooker reported one death due to perforation in 348,310 pregnancies.

The comparative incidence of peptic ulcer in males and females in various age groups is not only exceedingly interesting, but also throws some light on the possible etiological basis of the disease.

Sandweiss[11] found 101 cases of peptic ulcer prior to puberty with an incidence of 52 in males and 49 in females. This distribution is almost identical in menopausal women and in women in whom some mild endocrinopathy tending toward masculinity exists. About 50 per cent of 30 women investigated endocrinologically by Sandweiss were found to have either hypopituitarism or hypothyroidism, and the remainder were in a climacteric characterized by an abrupt onset or aggravation of their ulcer symptoms.

During the childbearing age, this fifty-fifty ratio between men and women is markedly altered. Available statistics indicate that adult males are afflicted four to five times more frequently than women in the childbearing age.

The exact incidence of peptic ulcer in man is not certain, but Portis and Jaffe[8] reported on 9,171 consecutive autopsies and found the incidence of active

or healed ulcers in white men and women to be 5.23 per cent and in Negroes 3.5 per cent. Other series show the incidence to be as high as 19 per cent. Since some heal without any scar the incidence most likely is higher. With the available statistics, however, the incidence of ulcers in all male adults is well over 10 per cent, and since they are afflicted about four to five times as frequently as adult females, the expected incidence in women in the childbearing age would be about 2 per cent.

Hurst and Stewart[5] suggested that the physiologic atony of smooth muscle which supposedly occurs during pregnancy, e.g., in the ureter, and the hypochlorhydria commonly seen during pregnancy might alter the conditions of hypermotility and hyperacidity so often present in ulcer patients.

The remarkable drop in the incidence of peptic ulcer during pregnancy and the childbearing age has encouraged some authors to advocate the use of female sex hormones in the treatment of peptic ulcer, but without noteworthy results.

A review of all the deliveries at Milwaukee County Hospital and seven other hospitals in Milwaukee for the years 1944 through 1953 was done to determine the incidence of peptic ulcer complicating pregnancy. Six cases of ulcer complicating pregnancy were found in 149,491 deliveries. One of these was fatal and is being reported as the eighteenth death due to peptic ulcer complicating pregnancy.

The patient, A. C., was a 37-year-old, married white woman, gravida vi, para v, who entered Milwaukee County Hospital at 9:46 P.M. on Nov. 6, 1953. Forty-five minutes prior to admission, the patient attempted to have a bowel movement and passed a large amount of blood, presumed to be from the vagina, collapsed, and was brought to the hospital with a tentative diagnosis of placenta previa.

Her last menstrual period was Jan. 4, 1953, and she had not been at the prenatal clinic in the outpatient department for this pregnancy, although she had been at the cardiac clinic for a heart murmur during January and March, 1953.

She had been at the hospital from Oct. 20 to Oct. 23, 1953, in false labor, and routine testing at that time revealed a 4 plus Wassermann and a strongly positive Kline test. During that admission she had normal blood pressure, had 2 plus pitting edema of the legs and gave a history of having "had the flu" three weeks previously with "quite a bit of heartburn." No other ulcer signs or symptoms could be elicited. She denied any hematemesis, melena, or bright red bleeding from the rectum.

She stated that she had had treatment for syphilis at the outpatient department, but a later review of her clinic chart failed to substantiate this. Syphilis had been diagnosed at the cardiac clinic, but she failed to keep the appointments for treatment, as well as at the cardiac clinic.

On admission, she was very pallid; the blood pressure was 96/58; pulse 130 per minute; respirations 20 per minute; temperature 97.2° F. orally; and she complained of abdominal cramps.

Examination revealed a loud Grade II-III systolic murmur over the entire precordium and a questionable diastolic murmur at the third intercostal space at the left sternal border. The abdomen showed a tumor of pregnancy; there were no contractions; the fetal position was right occipitoanterior; and the fetal heart tones were present in the right lower quadrant at 150 per minute. Dark red melena flowed from the rectum and there was no cervical dilatation or vaginal bleeding.

A tentative diagnosis of bleeding peptic ulcer was made despite the paucity of symptoms referable to ulcer.

She had one episode of hematemesis at 6:00 A.M. on the day following admission, and she continued to have moderate rectal bleeding. A transfusion of 1,500 c.c. of blood was given immediately and transfusions were continued at a slow rate during the remainder of the day, despite which the hemoglobin remained at 8.5 Gm. Other hematologic examination showed color index 0.84; erythrocyte count 3.23; leukocyte count 16,700, and stab forms 59 per cent.

Two days after admission, the patient had a very short, relatively painless labor and spontaneously delivered a 4 pound, 4 ounce male infant.

By the third hospital day, 10 pints of blood had been given, but the blood picture remained essentially the same. Surgery was advised, but both the patient and her husband refused. She finally consented to operation on the afternoon of the fourth hospital day after she had received a total of 15 pints of blood.

Fig. 1.

Fig. 2.

Fig. 1.—Dilated stomach showing the three acute ulcers and the one healed ulcer.
Fig. 2.—Closer view of the specimen showing the acute ulcers and the healed ulcer.

When the abdomen was entered, a greatly dilated stomach was found and both it and the bowel were filled with blood. At this point the patient went into shock and blood was given under pressure and vasopressors were given before the operation was continued. A gastrotomy was then done and three gastric ulcers were found, one of which contained a pipestem artery, actively bleeding. The patient went into cardiac arrest and prompt cardiac massage was instituted through an incision in the left chest wall. The heart responded for short intervals, but failed to do so after one hour and the patient was pronounced dead. She had received 3 pints of blood during operation.

An autopsy was performed and the findings were:

1. Three acute ulcers, not syphilitic, on the posterior wall near the greater curvature and approximately 12 cm. from the pylorus, measuring 8, 6, and 5 mm. in diameter, one containing a pipestem artery. There was also an old healed gastric ulcer on the posterior wall, 7 cm. from the cardia.

2. Old rheumatic heart disease with mitral stenosis.
3. Syphilitic aortitis and pulmonitis and mitral valvulitis.
4. Pyelonephritis of the right kidney with thickening of the right ureter with ureteritis.
5. Terminal glomerulitis.
6. Acute central necrosis of the liver and pericholangitis.
7. Acute splenitis and lipoid granulomas of the spleen.

The baby did well and was discharged from the hospital on Nov. 28, 1953, with a positive serologic test for syphilis. He is being followed at the pediatric clinic.

Summary

1. The literature concerning peptic ulcer complicating pregnancy has been reviewed and presented.

2. A statistical analysis of peptic ulcer complicating pregnancy for the years 1944 through 1953 in eight of the major hospitals in Milwaukee, comprising 149,491 deliveries, has been presented.

3. The equal incidence of peptic ulcer in males and females before puberty and after the climacteric has been indicated. Statistical verification of the relatively low incidence of peptic ulcer in adult females (1:5) has been presented.

4. The salutory influence of pregnancy on peptic ulcer is postulated.

5. A case of fatal hemorrhage from three bleeding gastric ulcers in a term pregnancy has been presented.

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MULTIPLE MIGRATORY THROMBOPHLEBITIS ASSOCIATED WITH OVARIAN CARCINOMA

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THE excellent review in 1938 by Sproul[1] first brought to light the frequent association of thrombophlebitis with cancer of the pancreas and other organs, but she stated that it did not occur with genital carcinoma. Since then two cases of ovarian carcinoma with multiple migratory peripheral thrombophlebitis have been reported.[2, 3] I submit a third case and also will point out some of the present concepts of the etiology of this phenomenon.

Case Report

Mrs. E. W., No. 112888, a 47-year-old married white woman, was perfectly well until Oct. 13, 1952, when she first developed a painless swelling in the right side of the neck. The patient also noted some engorgement of the superficial veins of the right side of the upper chest. On Oct. 20, 1952, the patient noted edema of the right arm with engorgement of the veins. She was seen by her local doctor, who made the diagnosis of thrombophlebitis of the superficial veins of the neck and arm. On Dec. 14, 1952, the patient developed swelling of the left leg and foot with a thrombus in a superficial dorsal vein of the foot. She had no other complaints. She stated she had lost approximately 60 pounds in the past year, but had been on a diet for that purpose. The only significant fact in her past history was a bilateral saphenous vein ligation in 1946. The last menstrual period was on Dec. 6, 1952.

Physical Examination.—The patient was an alert, slightly obese, white woman in no apparent distress. Her blood pressure was 120/78; temperature 98.0° F.; pulse 80 regular; respirations 18; weight 196 pounds. There was a slight fulness noted in the neck with moderate tenderness to palpation over the right superficial neck veins; the superficial chest veins were distended over the right upper chest anteriorly; the lungs were clear to auscultation and percussion; the heart was regular with no murmurs; the abdomen was obese, with no palpable masses, and soft, with slight tenderness in the right upper quadrant. There were no pudendal lesions. The vagina showed a parous introitus, slight cystocele and rectocele, no inflammation; the cervix was clean, smooth, and mobile, slightly pulled to the left; the uterus was in first-degree retroversion, symmetrical, firm, mobile, and of normal size. In the right adnexa there was an indistinct, 6 cm., smooth, soft mass present. In the left adnexa there was a fixed, nodular, irregular mass, approximately 5 cm. in diameter. By rectovaginal examination the left adnexal mass seemed to encroach upon the rectum, but the rectal mucosa felt intact. There was slight edema of the right arm with prominent superficial veins, and slight edema of the lower left leg and foot with a palpable thrombus in a superficial vein on the dorsum of the left foot. The reflexes were physiological. There were no palpable masses in the lymphatics.

Laboratory Findings.—On admission, the hemoglobin was 12.5 Gm.; the erythrocyte count was 4.31 million; the leukocyte count 8,600 with a normal differential. Urinalysis was negative. The sedimentation rate was 27 mm. in 45 minutes. The serologic test for syphilis was negative. Bleeding, coagulation, and prothrombin times were within normal limits. The blood sugar was 70 mg. per cent; nonprotein nitrogen 30 mg. per cent. The stools were negative for occult blood. The thymol turbidity and cephalin flocculation test were within normal limits. Total serum proteins and albumin-globulin ratio were normal. Serum phosphatase and serum lipase were within normal limits. Studies of the bone marrow

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showed it to be normal. The electrocardiogram was normal. X-ray studies of the chest were negative; excretory pyelograms were normal; cholecystograms and gastrointestinal series were normal.

Clinical Course.—The history of the marked weight loss and the migratory thrombophlebitis prompted a thorough work-up to rule out pancreatic or gastrointestinal-tract carcinoma. Sigmoidoscopic examination was done and no abnormalities were noted. The tentative diagnosis of either metastatic or primary ovarian carcinoma was made and on Jan. 21, 1953, an exploratory laparotomy was performed. On opening the abdomen, a small amount of straw-colored fluid was encountered. Examination of the pelvic organs showed a uterus of normal size. The left ovary was replaced by a 5 cm. cystic mass covered by small papillary projections which involved the right tube and were adherent to the peritoneum of the lateral pelvic wall. Frozen sections were made resulting in a tentative diagnosis of malignant cystadenocarcinoma. A bilateral salpingo-oophorectomy and total abdominal hysterectomy were performed. The tumor was adherent to the lateral pelvic wall on the right, so the area of involved peritoneum was widely excised after the ureter was exposed. A small portion of adherent omentum was also excised. The postoperative course was uncomplicated. Postoperatively, a course of deep x-ray therapy was given. The final pathological diagnosis was bilateral papillary serous cystadenocarcinoma of the ovaries with extension to the right tube and pelvic peritoneum.

The peripheral thrombophlebitis cleared slowly following operation and no further attacks occurred. The patient has been followed closely in the outpatient clinic and has fully recovered. She was last seen April 21, 1954. At that time she stated she felt fine and there was no evidence of thrombophlebitis or recurrence of the cancer.

Comment

Many theories have been presented to explain the phenomena of venous thrombosis from cancer. Still the cause of the thrombosis is not definitely known. There is ample proof that the thrombosis is not due to tumor emboli.[1] Recent workers have postulated that a toxic product from the tumor produces some alteration in blood-clotting mechanisms.[4-8] Trypsin was thought to be the cause of the thrombosis in pancreatic carcinoma, but the work of Ratnoff[9] tends to disprove this theory.[9] It is interesting to note that many of the tissues from which arise neoplasms that are associated with thrombosis have high thromboplastic activity.[10] Very possibly thromboplastin or a substance with thromboplastic activity could be the cause of the thrombosis in all cancers. Study of all tumors with associated thrombophlebitis for their thromboplastic activity would be of value. We have tested one cystadenocarcinoma from a patient without thrombosis and the thromboplastin levels were negligible. We hope to make further thromboplastin determinations on carcinomas from patients with thrombophlebitis.

I am indebted to Dr. Robert D. Koler of the University of Oregon Medical School for making the thromboplastin determinations.

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Department of Reviews and Abstracts

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Selected Abstracts*

Münchener medizinische Wochenschrift

Vol. 96, No. 11, March 12, 1954.

*Schmidt, H. J.: The Gynecologist and Prophylaxis of Dental Caries, p. 297.

Schmidt: Gynecologist and Dental Caries, p. 297.

It is maintained that dental health and fluorine are closely related. Fluorine is transmitted through the placenta and excreted in the milk. Hence the author suggests that the dental health of infants and children can be influenced significantly by ensuring adequate fluorine intake in pregnant women and nursing mothers. This can be done through fluoridation of the water supply, the use of pills, and the proper treatment of table salt.

WALTER F. TAUBER, M.D.

Vol. 96, No. 13, March 26, 1954.

*Mayer, A.: Comments on Psychogenic Sterility, p. 345.

Vol. 96, No. 14, April 2, 1954.

*Mayer, A.: Comments on Psychogenic Sterility (Conclusion), p. 378.

Wisotzky, G.: Experiences With Tokofinal, an Oxytocic, p. 383.

Mayer: Psychogenic Sterility, p. 345 and p. 378.

In the first article the physiologic and anatomic factors of conception are discussed. It is pointed out that psychic factors are well known to affect the menstrual cycle. Emotional disturbances influence peristalsis and even patency of the Fallopian tubes. So, we see that functional occlusion can prevent fusion of the gametes, on the one hand, and excess motility can bring the ovum to the endometrial cavity before it is capable of nidation, on the other. The author further mentions the influence of emotional upset on vaginal pH and the tenacity of the mucus plug in the cervix. He also feels that psychological factors may be involved in the formation of defective ova and sperm.

In the second article, the psychiatric aspects are discussed. Fear of coitus can lead to vaginismus. This can be treated by judicious use of pelvic examination, to convince the patient that vaginal distention need not be painful. While frigidity is not in itself a bar to conception, it should be considered as a factor when a "low fertility index" is already present for other reasons. Lack of peace of mind during coitus can prevent conception. It is pointed out that there are many cases of "trying too hard." The author cites cases where pregnancy followed closely on the removal of stress, as for instance, by the adoption of a child. On the other hand, he also mentions unions in which the desire not to have more children acts as a sole and effective contraceptive agent although children were previously born of the marriage.

WALTER F. TAUBER, M.D.

*Titles preceded by an asterisk are abstracted below.

Vol. 96, No. 15, April 9, 1954.

Mayer, A.: Legal and Psychological Problems of Artificial Insemination, p. 393.

Vol. 96, No. 16, April 16, 1954.

Mayer, A.: Legal and Psychological Problems of Artificial Insemination (Conclusion), p. 444.

Vol. 96, No. 20, May 14, 1954.

Bingold, K., and Stich, W.: The Treatment of Iron Deficiency Anemia, p. 586.

Vol. 96, No. 25, June 18, 1954.

*Grauert, H.: Etiology and Treatment of Eclampsia, p. 719.

Samuels, J.: On a Rational Therapy of Cancer With Short-Wave Treatment of the Pituitary and Gonads, p. 724.

Wening, H.: Early Diagnosis of Carcinoma of the Female Genital Tract in Clinical and Office Practice, p. 730.

Grauert: Etiology and Treatment of Eclampsia, p. 719.

The author adduces proof from clinical comparisons and autopsy material that the clinical picture of eclampsia reflects cyanide poisoning. Cyanide is a normal by-product of gastric digestion which, in normal metabolism, is rapidly detoxified to thiocyanate. In severe toxemia the detoxification mechanism is, for an as yet obscure reason, inoperative. Based on this theoretical background, the author proposes to treat eclampsia and severe pre-eclampsia with sodium thiosulfate intravenously in 50 per cent aqueous solution in 2 c.c. dosage, diluted in 10 c.c. of 20 per cent glucose. Depending on the severity of the case, the treatment should be undertaken between once every other day and twice a day. Intramuscular administration is possible, but the intravenous route is to be preferred. An admittedly small series of 34 cases of eclampsia treated in this manner by the author is presented. Results are divided into: excellent effect 21, good effect 8, moderate effect 3, no change 2.

WALTER F. TAUBER, M.D.

Vol. 96, No. 26, June 25, 1954.

Samuels, J.: On a Rational Therapy of Cancer With Short-wave Treatment of the Pituitary and Gonads (Conclusion), p. 756.

Vol. 96, No. 31/32, July 30, 1954.

Neudecker, L.: A Contribution to the Treatment and Prevention of Puerperal Mastitis, p. 893.

Pickl, H.: The Action of Testosterone in Prolonging Life in Metastases From Carcinoma of the Breast, p. 894.

Vol. 96, No. 33, Aug. 13, 1954.

Hoecht, H.: On a Preparation Containing Rauwolfia and Its Action on Hypertension, p. 923.

Vol. 96, No. 35, Aug. 27, 1954.

Schultze-Jena, E.: Congenital Malformation of the Lumbar Spine in Mother and Child, p. 980.

Vol. 96, No. 36, Sept. 3, 1954.

*Plattner, P., and Hadavi, S.: The Richardson Test for Pregnancy and Sex of the Unborn Child, p. 1020.

Hilber, H., and Mentz, B.: Nutrition in Pregnancy and Infant Health, p. 1027.

Plattner and Hadavi: Richardson Test for Pregnancy and Sex of Unborn Child, p. 1020.

The dinitrophenylhydrazine urine test for pregnancy and the saliva test for infant sex are re-evaluated. Eighty per cent positive correlation is obtained. This is regarded as unsatisfactory for a test of this sort.

WALTER F. TAUBER, M.D.

Surgery, Gynecology and Obstetrics

Vol. 98, No. 4, April, 1954.

Allison, Rhoda: A Modification of the Galli-Mainini Pregnancy Test Using Serum and the Diffusion Enzyme Hyaluronidase, p. 446.

*Douglas, Gordon Watkins: Observations on the Pathology of Primary Carcinoma of the Vagina and Its Relation to Therapy, p. 456.

Collins, Conrad G., Burman, R. G., and Tucker, G. W.: Enzymatic Débridement (Streptokinase and Streptodornase) in the Treatment of Pelvic Abscesses, p. 467.

Johnson, C. G.: Ectopic Pregnancy, p. 481.

Douglas: Pathology of Primary Carcinoma of Vagina and Its Relation to Therapy, p. 456.

During the period 1944 to 1952, the incidence of vaginal carcinoma was 0.04 per cent and the ratio of vaginal to cervical carcinoma was 1:67 on the gynecological service of Bellevue Hospital. Of the 8 cases reported on, 5 were of the everting type, with 4 of them arising in the posterior vaginal wall and one on the right lateral wall. Two were of the infiltrating type and were extensive tumors of the anterior vaginal wall with infiltration of the bladder. One was of the surface type and arose in the posterior fornix.

The everting forms seldom showed lateral growth and distended the vaginal wall without deep invasion. Microscopically, they were generally well-differentiated papillomatous growths and their growth, judged by tissue reaction, was considered to be slow. The infiltrating forms exhibited considerable lateral spread but little growth into the vaginal lumen. Microscopically, they were highly anaplastic tumors. The surface type had marked lateral growth but little if any invasion, being confined mostly to the mucous membrane and well differentiated. It was noted that on microscopic examination of all three types the tumor extended beyond the described vaginal limits in four of the eight cases either by surface or subepithelial lateral spread. On the other hand, the marked thickening and induration of the rectovaginal septum and parametrial tissues which occur with primary carcinomas of the vagina make clinical staging of the disease such as that prescribed by Courtial difficult and somewhat unreliable.

All 8 cases were treated surgically and the operations were planned individually as curative rather than palliative procedures. Pelvic exenteration with vulvectomy was carried out in one case; radical hysterectomy was performed four times and vaginal hysterectomy once. In two other cases the uterus had been removed previously. In addition to the exenteration, removal of the bladder was done in two cases. The rectum was excised in one case for recurrence following the primary operation. Total colpectomy was carried out three times and partial colpectomy (with removal of most of the vagina) five times. Removal of the parametrial, obturator, hypogastric, and external iliac nodes was done in six cases and in none of the nodes were metastases encountered. The failure to find parametrial and pelvic lymph node involvement is directly opposed to the previously reported high clinical estimates of the spread of the disease. The discrepancy may very well be on the basis of the marked amount of inflammatory induration previously alluded to in the preceding paragraph. The series is much too small to arrive at a conclusion regarding the frequency of lymphatic spread to regional nodes and the stage of the disease at which it occurs, but it would appear to be less frequent and a later manifestation than is currently accepted. It can be inferred that complete surgical removal of the tumor will give a good chance of cure even when the primary lesion is large and involves contiguous structures. Accordingly, it is the author's opinion that every patient with primary carcinoma of the vagina be considered as a candidate for radical surgery. Results from radiation treatment and incomplete surgery have not been encouraging.

VINCENT TRICOMI, M.D.

Vol. 98, No. 5, May, 1954.

Hickey, R. C., and Keettel, W. C.: Some Hormonal Aspects of Human Parturition With Particular Reference to the Neurohypophysis, p. 541.

Binder, S.: Placenta Previa and Previous Lower Segment Cesarean Section, p. 625.

Vol. 98, No. 6, June, 1954.

Dalali, S. J., Plentl, A. A., and Bachman, A. L.: The Application of Pelvic Venography to Diagnostic Problems Associated With Cancer of the Female Genital Tract, p. 735.

*Jeffcoate, T. N. A., and Roberts, H.: The Effects of Urethrocystopexy for Stress Incontinence, p. 743.

Jeffcoate and Roberts: Effects of Urethrocystopexy for Stress Incontinence, p. 743.

This is a report on the effects of urethrocystopexy for stress incontinence in 24 women as demonstrated by cystourethrography. In 15 of the cases comparable observations were also made preoperatively. All but two of the women had previously been operated on unsuccessfully by the vaginal route; 12 once, 4 twice, 4 three times, and 2 four times. All cases examined roentgenologically preoperatively showed evidence of loss of the posterior urethrovesical angle when the woman was straining and sometimes even when she was at rest.

The Marshall-Marchetti-Krantz operation was performed in 19 cases and there were 2 failures (2 and 6 months after operation) in addition to 4 cases of prolonged difficulty of micturition. The latter were considered to be on the basis of excessive elevation of the urethrovesical function. The Williams technique was used in 5 cases with 2 cases of almost immediate failure.

The most constant feature of successful cases was the restoration of the posterior urethrovesical angle and not, as is often stated, elevation of the urethra and bladder base. This corroborates the authors' previous conclusions about the importance of the posterior urethrovesical angle in the maintenance of urinary continence. Simultaneously they emphasize that continence, or lack of it, does not always depend on the angle. They feel however, that it is a feature in at least four out of every five cases of stress incontinence.

VINCENT TRICOMI, M.D.

Vol. 99, No. 1, July, 1954.

*Newton, Michael: Use of Matched Pairs of Cases to Compare Treatment by Surgery or Radiation, p. 29.

Newton: Use of Matched Pairs of Cases to Compare Treatment by Surgery or Radiation, p. 29.

A study in which 15 patients with early carcinoma of the cervix, who were treated primarily by radical surgery at the Hospital at the University of Pennsylvania, were matched with 15 patients who were treated primarily by radiation at the same hospital over the same period of time, namely, November, 1948, through October, 1953.

The method of employing matched pairs of cases, one not commonly used in medical studies, was followed in order to obviate some of the familiar difficulties encountered with other techniques of study. It is felt that by employing such a method a smaller number of cases would be needed to obtain meaningful results since each pair, in effect, represents a separate experiment.

In this study the patients were matched for (a) presence of invasive carcinoma of the cervix on pathologic examination; (b) stage of disease on initial examination (League of Nations classification); (c) age; (d) date of initial treatment.

Over a follow-up period averaging 26 months there was little difference found between the two groups with respect to survival, recurrence of disease, and the incidence of early or late complications of treatment.

VINCENT TRICOMI, M.D.

Vol. 99, No. 2, August, 1954.

Lisa, J. R., Gioia, J. D., and Rubin, I. C.: Observations on the Interstitial Portion of the Fallopian Tube, p. 159.

Vol. 99, No. 5, November, 1954.

*Graham, J. B., Graham, R. M., and Liu, W.: Prognosis in Cancer of the Uterine Cervix Based on the Vaginal Smear Before Treatment; SR—The Sensitization Response, p. 555.

Graham, Graham, and Liu: Prognosis in Cancer of Cervix Based on Vaginal Smear Before Treatment, p. 555.

This study constitutes an analysis of the pretreatment vaginal smears in 136 patients with carcinoma of the cervix treated radiologically, and 103 patients treated surgically and followed for five years. The conclusion arrived at by the authors is that a marked sensitization response (SR) and, to a less extent, the presence of many basal cells indicate a favorable prognosis when treated surgically. The reverse is found in those with a poor SR, for the five-year survival rate is significantly better in the surgical group than in the radiologic group. The SR then is a useful prognostic index.

VINCENT TRICOMI, M.D.

Proceedings of the Society for Experimental Biology and Medicine

Vol. 85, No. 4, April, 1954.

Barraclough, C. A., and Leathem, J. H.: Infertility Induced in Mice by a Single Injection of Testosterone Propionate, p. 673.

Constant, M. A., and Phillips, P. H.: Effect of Diet and Trace Minerals on Erythrocyte Fragility and X-irradiation Mortality in Rats, p. 678.

Eskelson, E. D., Firschein, H. E., and Jensen, H.: Effect of Epinephrine on Thyroid Hormone Level in Blood, p. 637.

Fleischmann, W., and Nimaroff, M.: Combined Effects of X-irradiation and Testosterone Propionate on Accessory Sex Organs, p. 655.

*Ullberg, S.: Autoradiographical Distribution and Excretion Studies With S^{35}-Labelled Penicillin, p. 550.

Ullberg: Autoradiographical Distribution and Excretion Studies With S^{35}-Labelled Penicillin, p. 550.

A method of tracing the distribution of penicillin after intravenous injection, using radioactive sulfur, S^{35}, is presented. Heretofore bacteriological methods were the only means available for this type of study.

Radioactive penicillin (S^{35} labeled) was prepared biosynthetically and injected into a tail vein of mice in given dosages. The animals were killed at different times, the tissues rapidly frozen, and contact autoradiographs obtained showing the distribution of the tagged penicillin in the various tissues.

Distribution to normal tissues from the blood stream was found to occur rapidly. The greatest concentrations were found in the kidneys and the liver. The kidneys are responsible for the elimination of most of the penicillin, but the liver also rated high as an excretory organ, judging by the high activity in the biliary system. The subcutis and the lungs showed high concentrations; skeletal muscle and compact bone showed low concentrations; brain and cerebrospinal fluid, even lower concentrations.

An excellent photograph is reproduced showing the results of injecting a pregnant mouse with tagged penicillin. The autoradiograph showed high activity in the uterine wall, low in the fetus, and almost nonexistent in fetal fluids. Fetal brain contained essentially

less than other parts of the fetus, an indication that the blood-brain barrier functions even at this early stage. This method is applicable to the study of penicillin distribution in diseased tissue and, accordingly, the diffusion of labeled penicillin into an abscess is observed. The effect of probenecid, its inhibitory action on the renal excretion of penicillin, is demonstrated. Probenecid is one of the most promising of a number of compounds that block the renal excretion of penicillin. The autoradiograph shows a high degree of activity in the glomeruli against a background of relatively penicillin-free tubuli supporting the interpretation that this substance inhibits tubular secretion while glomerular filtration continues as usual.

These observations using the autoradiographical method correlate well with the observations that have been made using the microbiological assay for penicillin.

GEORGE D. SOLISH, M.D.

Vol. 86, No. 3, July, 1954.

Beher, W. T., and Anthony, W. L.: Effect of Dihydrocholesterol and Soy Bean Sterols on Elevated Tissue Cholesterol, p. 589.

Bragdon, E. D., Lazo-Wasem, E. A., Zarrow, M. X., and Hisaw, F. L.: Progesterone-Like Activity in the Plasma of Ovoviviparous Snakes, p. 477.

*Nelsen, C. D., Hunter, C. B., and Plentl, A. A.: Rate of Exchange of Sodium and Potassium Between Amniotic Fluid and Maternal System, p. 432.

Wachstein, M., and Lobel, S.: Abnormal Tryptophan Metabolites in Human Pregnancy and Their Relation to Deranged Vitamin B_6 Metabolism, p. 624.

Nelsen, Hunter, and Plentl: Rate of Exchange of Sodium and Potassium Between Amniotic Fluid and Maternal System, p. 432.

A dynamic steady state, in all probability, exists between the electrolytes of amniotic fluid and those of the maternal plasma, analogous to the electrolyte equilibrium of lymph cerebrospinal and extracellular fluid. The pathological depletion or accumulation of water in these hypothetical compartments is associated with or conditioned by a disturbance in the electrolyte transfer, changes in hydrostatic pressure, and the osmotic equilibrium. It was felt that a study of the exchange rates of sodium and potassium would be worth while and a comparison of these rates could be used to evaluate the hypothesis that the amniotic fluid is not a transudate or formed by the ultrafiltration of plasma.

Applying the mathematical theory of a multicompartment system and with the use of tracer substances, multiple simultaneous experiments were performed using isotopes of hydrogen, sodium, and potassium to determine the rate of exchange of these substances.

Two pregnant volunteers near term, in whom abdominal delivery was considered, were used. Na^{22} and deuterium oxide were introduced into the amniotic fluid by transabdominal puncture, Na^{24} was injected into the maternal system. Samples of amniotic fluid and maternal blood were collected at predetermined intervals and the concentration of tracers determined. The exchange rate of sodium to and from the amniotic fluid was thus obtained. This rate of exchange in opposite directions was found to be 15 and 16 meq. of sodium per hour, respectively.

In a second experiment deuterium oxide, Na^{22}, and K^{42} were simultaneously administered into the amniotic sac and the transfer rates of these substances from the amniotic fluid to the maternal system determined. The exchange rates were—31.9 moles of water, 0.014 mole of sodium and 0.00041 mole of potassium per hour.

It was concluded that water and electrolytes of the amniotic fluid are in dynamic equilibrium with maternal plasma and that each of these exchange at their own characteristic rates.

GEORGE D. SOLISH, M.D.

Journal of the Philippine Medical Association

Vol. 30, No. 5, May, 1954.

Sta. Cruz, Juan Z.: The Pathology of Endometrial Scrapings, p. 203.

Public Health Reports

Vol. 69, No. 9, September, 1954.

*Sowder, Wilson T.: Why Is the Sex Difference in Mortality Increasing? p. 860.

Sowder: Why Is Sex Difference in Mortality Increasing? p. 860.

Dr. Sowder points out that while the death rates for both males and females have decreased markedly in the United States in the past twenty years, the proportionate decrease for females has been considerably greater than that for males. In 1920 the excess of the white male death rate over the white female death rate was 8 per cent; it was 21 per cent in 1930; 32 per cent in 1940; and had risen to 49 per cent in 1950. These figures are for the United States. The author is particularly concerned with the state of Florida, where he is the State Health Officer. In his own state the corresponding excess of male rate over female rate for the corresponding years was 14 per cent, 34 per cent, 53 per cent, and 62 per cent.

It might be thought that these over-all rates hide some peculiarity associated with age at death. Therefore, the author has presented a table which demonstrates that, regardless of the "age specific death rate," in all age categories the percentage excess of male rate over female rate is greater for the year 1950 than it was for the year 1920. In some cases this change in percentage excess is quite marked. For example, in the age group 15 to 24 years, the percentage excess in 1920 was minus two (the female rate was greater than the male rate), while in 1950 the excess was 114 per cent (the male rate was more than twice that of the female rate). Dr. Sowder has some very interesting "speculations and suggestions" concerning this pattern. The following may be quoted: "The facts raise the suspicion that men are suffering from the very ancient illusion that they are the stronger and superior sex, when, as a matter of fact, we can only be sure that skeletal muscles are stronger. In past ages a big biceps counted a great deal in the battle of survival, but it means little now." In closing, the author makes a plea for more basic research into this alarming pattern.

SCHUYLER G. KOHL, M.D.

The Lancet

Vol. 267, Sept. 18, 1954.

*Evans, Gwilym: Hazards of Surgical Induction of Labour, p. 564.
(No author named) Blood Supply of the Pituitary Gland, p. 584.
(No author named) Placentography, p. 585.

Evans: Hazards of Surgical Induction of Labour, p. 564.

This series is based on 861 surgical inductions of labor (843 cases) that occurred in the 25,960 pregnancies attended in Guy's Hospital from 1928 to 1952. Prior to 1935, surgical induction was usually performed by the insertion of a tube, bladder, or bougie. Since then, amniotomy has been most commonly practiced. Of the 843 mothers, 7 died, one of postpartum hemorrhage, one of eclampsia, two of pulmonary embolus, one of hemorrhage from placenta previa, one of sepsis and one unknown.

The morbidity of this procedure is estimated to be 10.8 per cent (15 per cent of the primigravidas and 7.2 per cent of the multigravidas). The etiology of the fever was the same in both the primiparous and multiparous patients; birth canal infection accounted for 49.4 per cent and urinary tract infection for about one-third of the cases. The method of induction did not influence morbidity, but the longer the induction-delivery interval, the greater the morbidity. The stillbirth rate was 11.8 per cent and the neonatal death rate 3.8 per cent. There were 17 instances (2.02 per cent) in which the induction of labor was considered to be responsible for the fetal death—including 4 deaths from infection and 11 from prolapse of the cord. The latter is the great hazard of induction, occurring in 3.3 per cent of cases. The author notes that the position of the head influences the incidence of complications following surgical induction. If not engaged, maternal morbidity is increased by the extended time of delivery and fetal mortality is increased by the greater possibility of prolapse of the cord.

DAVID M. KYDD, M.D.

Vol. 267, Oct. 2, 1954.

*MacLeod, Malcolm: Rheumatic Heart-Disease in Pregnancy, p. 668.

*Millen, J. W., Woollam, D. H. M., and Lamming, G. E.: Congenital Hydrocephalus Due to Experimental Hypovitaminosis A, p. 679.

*Douglas, J. W. B.: Birth-Weight and the History of Breast-Feeding, p. 685.

MacLeod: Rheumatic Heart-Disease in Pregnancy, p. 668.

One hundred pregnant patients with rheumatic heart disease (28 mild, 60 moderate, and 12 severe cases) are reported. No maternal deaths occurred, but there were 3 neonatal deaths and 1 stillbirth. The author stresses the importance of pulmonary hypertension and efficient treatment of acute pulmonary edema. Spontaneous delivery was allowed in 72 instances. There were 7 cesarean sections and 12 therapeutic abortions performed.

DAVID M. KYDD, M.D.

Millen, Woollam, and Lamming: Congenital Hydrocephalus Due to Experimental Hypovitaminosis A, p. 679.

Using female rabbits deprived of vitamin A for periods up to 38 weeks, the authors have extended their earlier studies (Lancet 265: 123, 1953). In 47 of the 51 young examined, hydrocephalus was present. In severe instances the hind part of the cerebellum and of the medulla oblongata was displaced into the cervical canal. This was not true in the milder instances, with the conclusion that the displacement is secondary to the dilation of the lateral and third ventricles. The aqueduct was small but no smaller than that in control animals and the fourth ventricle was normal. No evidence of overgrowth of bone was found. To the other congenital abnormalities that have been previously reported, associated with vitamin A deficiency, hydrocephalus is therefore added. The authors suggest the possibility that overproduction of cerebrospinal fluid rather than obstruction may be the cause of the hydrocephalus. The small aqueduct that occurs in both control and deficient fetuses may be relatively insufficient in the latter. Possible modes of development are discussed.

DAVID M. KYDD, M.D.

Douglas: Birth-Weight and History of Breast-Feeding, p. 685.

This is a statistical analysis purporting to show that women who are successful in breast-feeding one child are less likely to have subsequent children below birth-weight (less than 6 pounds) than are those who are unsuccessful in breast-feeding the previous child.

DAVID M. KYDD, M.D.

Vol. 267, Oct. 9, 1954.

*Wilson, L. A., Auld, W. H. R., and Bowman, W.: Incomplete Pituitary Insufficiency, p. 715.

Wilson, Auld, and Bowman: Incomplete Pituitary Insufficiency, p. 715.

Eight (1 male and 7 female) patients who had suggestive but varied symptoms of hypopituitarism were studied. The basal metabolic rate, water excretion (Kepler), urinary 17-ketosteroid excretion, the serum cholesterol concentration, and the insulin tolerance were determined. The first three results were usually abnormal, the latter two were usually normal. Testosterone administration was the principal therapeutic measure. The authors note that such incomplete syndromes may be difficult to confirm.

DAVID M. KYDD, M.D.

Proceedings of the Staff Meetings of the Mayo Clinic

Vol. 29, No. 20, Sept. 29, 1954.

*Martin, William J., Sittel, John A., Jr., Nichols, Donald R., and Geraci, Joseph E.: Bacteremia Caused by Aerobacter Aerogenes: Review of 20 Cases, p. 541.

Martin, Sittel, Nichols, and Geraci: Bacteremia Caused by Aerobacter Aerogenes, p. 541.

Review of the literature reveals 34 cases of bacteremia due to *Aerobacter aerogenes.* This report deals with 20 additional cases from the Mayo Clinic from 1940 to 1954. The sex incidence was three males to one female and the age distribution ranged from 2½ to 86 years. As in the previously reported series, the most common portal of bacterial entry was via the urinary tract; 75 per cent of these patients were infected in this way. Sixty per cent of the infections followed some type of surgical or manipulative operation. Diabetes seemed to be a factor in 3 instances. There were 3 deaths in the series.

The clinical picture was characterized by fever, with a proportional pulse rate, chills, sweating, prostration, albuminuria, and leukocytosis.

Streptomycin-sensitivity studies were conducted on 19 patients and 15 were found resistant, whereas but 2 of 15 tested showed resistance to the tetracyclines. Mention is made of employing Polymyxin B sulfate with success in 3 cases. It is felt, however, that this compound is too toxic for routine use.

The recommended treatment consists of 1 Gm. of either streptomycin or dihydrostreptomycin, or 0.5 Gm. of each every 12 hours and 750 mg. of a tetracycline compound every six hours until three blood cultures are negative.

ARTHUR PERELL, M.D.

Fertility and Sterility

Vol. 5, No. 5, September—October, 1954.

*Hammen, Richard, Schultz-Larsen, Jorgen, and Carlsen, F. E.: Electron Microscopy of Human Spermatozoa, p. 411.

de la Balze, F. A., Mancini, R. E., Bur, G. E., and Irazu, J.: Morphologic and Histochemical Changes Produced by Estrogens on Adult Human Testes, p. 421.

Collett, Mary E., Wertenberger, Grace E., and Fiske, Virginia M.: The Effect of Age Upon the Pattern of the Menstrual Cycle, p. 437.

Hendricks, Charles H., and Zuspan, Frederick P.: The Possible Role of Hyperheparinemia in the Infertile Couple, p. 449.

Byron, Charles S., and Pearl, Herbert: Cushing's Syndrome: Cure and Subsequent Pregnancies Following Removal of an Adrenocortical Adenoma, p. 455.

Bayer, Leona M.: Potential Infertility in Young Women: Medical Alertness vs. Patient Anxiety, p. 461.

Rozin, Samuel: Genital Tuberculosis, p. 468.

Hafez, E. S. E.: Infertility in Buffalo Cows: Physiologic and Anatomic Considerations, p. 482.

Hammen, Schultz-Larsen, and Carlsen. Electron Microscopy of Human Spermatozoa, p. 411.

Visualization of human spermatozoa with the electron microscope has not been very satisfactory. This is owing to the large amount of detritus in the seminal fluid and the relatively low density of the poorly transparent spermatozoa. By means of a special technique of washing, drying, and cutting the specimens, the authors have managed to overcome these difficulties. As a result, they have seen details heretofore unobserved. These concern the tail, the middle piece, the neck, and the head, all of which present a rather complex composition. This is readily seen in the amazingly clear photomicrographs. The revelations of the electron microscope bring forth a completely different concept of the structure of spermatozoa. They also provide an insight into the cytology of the future.

P. TOPKINS, M.D.

Correspondence

Epidural Injection of Normal Saline to Prevent Spinal Headache

To the Editors:

In reference to the article "Epidural Injection of Normal Saline as a Means of Prevention of Spinal Headache," written by L. B. Mehl, M.D., appearing in the October, 1954, issue of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, pages 1105-1108, we wish to point out that Dr. Mehl omitted reference to our original work on this technique.

Dr. Mehl states: "At this hospital, another method of preventing escape of spinal fluid following administration of saddle block was thought possible, namely, the injection of normal saline epidurally at the site of, and immediately following, the administration of the spinal anesthetic."

In our series, the prevention of headache following spinal anesthesia by the use of epidural solution at the time of the spinal anesthesia procedure was proposed.[1] To be sure, Dr. Mehl's series included patients undergoing obstetrical procedures. Our series included all types of surgical and obstetrical procedures. It is felt, however, that the credit of using this technique for the first time in preventing spinal headache should be given to us.

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Reference

1. Kaplan, M. S., and Arrowood, J. G.: Anesthesiology 13: 103, 1952.

Eclampsia Treated With Chlorpromazine

To the Editors:

During an extensive pharmacological investigation Courvoisier and associates in 1953 found that chlorpromazine (3-chloro-10[3'-dimenthylaminopropyl] phenothiazine*) abolished the pressor reflex elicited by electrical stimulation of the central end of the vagus nerve. Dasgupta, Mukherjee, and Werner in 1954 observed that chlorpromazine effectively suppressed the "sham rage" of diencephalic animals. It was therefore concluded that chlorpromazine could block certain hypothalamic responses and that a severance of corticohypothalamic tracts made such an action apparent. These observations have been utilised in treating eclampsia with chlorpromazine by blocking certain hypothalamic responses.

During the period of October, 1954, to February, 1955, 38 cases of eclampsia were treated with chlorpromazine. The schedule of treatment is as follows:

At the beginning, 25 mg. of Largactil and 25 mg. of Phenergan,† intravenously; at the end of the first hour, 25 mg. of Largactil, intramuscularly, plus 5 c.c. calcium gluconate (10 per cent) and 50 c.c. glucose (50 per cent), intravenously; at the fifth hour, 25 mg. of

*4560 R.P., Largactil—N. D. Spécia, Paris.
†N–(2'-dimethyl-2'-methylethyl) phenothiazine hydrochloride.

Largactil and 25 mg. of Phenergan, intramuscularly; at the twelfth hour, 25 mg. of Largactil, intramuscularly; at the twentieth hour, 25 mg. of Largactil and 25 mg. of Phenergan, intramuscularly.

Only one of 38 patients treated died and 10 babies (the fetal heart sounds of whom could not be heard before the treatment was instituted in 9 cases) were born dead. In this series 32 were primigravidas; 12 had antepartum, 18 intrapartum, and 8 postpartum eclampsia. Nine patients had more than 10 fits and 8 over 20 fits before treatment. After the treatment was started, there were less than 10 fits in 28 cases and more than 10 fits in the remaining 10 cases. The range of fall of blood pressure was variable. The drop in the first hour after the treatment varied from nil to 80 mm. Hg, the average being 36 mm. Hg. Psychosis developed in 4 patients. In two it lasted for four days and in the other two for thirty days.

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Dasgupta, S. R., Mukherjee, K. L., and Werner, G.: Arch. internat. pharmacodyn. **97**: 149, 1954.

Etiology of Toxemia

To the Editors:

In the March issue of your Journal, Dr. E. W. Page and Dr. Mary B. Glendening have provided invaluable and unique data affording a deeper understanding of the aetiological problems of toxaemia. Obstetricians would readily agree with the conclusions, implicit in their experimental findings, that (1) reduction in the renal blood flow and in glomerular filtration, synonymous with renal ischaemia, occurs in pre-eclampsia and that (2) "sodium itself plays the final determinate role in causing the entire syndrome." Although from their experiments we are forced to admit that DCA facilitated the occurrence of the eclampsia-like syndrome, there are many reasons which could be advanced to exclude corticoids from primary aetiological significance in the human disease and even to deny to DCA an essential responsibility in equivalent experiments.

Renin is not invariably a diuretic in laboratory animals. A sharp fall in urine volume follows immediately on its injection into normal dogs and even those afflicted with diabetes insipidus. It effects this change by reducing the glomerular filtration rate and the renal blood flow.[1] In rabbits a dose smaller than 1 unit has a slight antidiuretic effect.[2] Its renal haemodynamic action has been investigated by angiography and unquestionable evidence is to hand indicating that it provokes ischaemia of the cortex.[3]

When this renal change is accompanied by an excessive salt intake *and presumably without any increased corticoid outpouring,* an eclampsia-like syndrome can be elicited both in man and in the laboratory animal. Byrom,[4] causing renal ischaemia to occur by the application of the Goldblatt clamp to the pedicle of uninephrectomised rats, nurtured on saline, has evoked not only severe hypertension and fits, but on occasion swift and profound oedema. Likewise Dieckmann,[5] when employing intravenous saline in the therapeusis of anuria—a condition in which renal ischaemia is undeniable—caused severe hypertension, acute oedema, and convulsions to occur in his patients. Both these examples of severe renal ischaemia, in association with NaCl presumably in excess, become responsible for the provocation of an eclampsia-like syndrome similar to that described by Drs. Page and Glendening and yet without the intrusion of any recognisable corticoid influence. Since renin can produce renal ischaemia it may be inferred that in association with NaCl alone it could give rise to like manifestations independent of corticoid intervention. With regard to oedema formation,

much evidence has been adduced to show that a reduced glomerular filtration alone can effect NaCl and water retention.[6] Especially is this to be appreciated when it is recognised that a 1 per cent reduction in glomerular filtration rate, an amount frequently undetectable, can become responsible for the retention of 11 Gm. of sodium per day,[7] a not inconsiderable amount if considered against the period of pregnancy. The occurrence of proteinuria as a result of renal ischaemia and the production of hypertension based on the same cause, provided the NaCl environment is adequate, is easier to comprehend. The single process, renal ischaemia, can therefore suffice to explain the eclampsia-like syndrome.

The contention that corticoids intrude into the aetiology of pre-eclampsia is assailable on many grounds. These hormones are generally held merely to possess a regulatory function in regard to the metabolism of electrolytes and water. Even in the case of aldosterone, the most potently salt retaining amongst them, its exhibition in a patient with Addison's disease maintained on DCA resulted in both an initial *diuresis* and a salt *loss*.[8] Then again the blood level of these substances reflected in the urine of the toxaemic bears no strict relationship to the severity of the disease. In fact, Venning[9] has shown that an actual reduction in their amounts occurs as the syndrome mounts. Whereas it is usual as a corticoid effect to encounter a potassium loss with a sodium retention,[10] no such change has been detectable in the toxaemic patient.[11] Above all, an explanation of the relative freedom of pregnancies other than the first from pernicious corticoid effects is difficult if not impossible to formulate.

The challenge to a thesis propounding placental influences in the production of toxaemia is even more formidable, for toxaemia can occur subsequent to the birth of the placenta, or can recur in labour following a period of quiescence coincident with the death of the foetus, an intermission quite inexplicable on a placental thesis of aetiology. The cause of the renal ischaemia responsible for the eclamptic syndrome cannot reside in the placenta therefore.

The renal change has been shown experimentally in animals to accompany both the resistance of the myometrium to stretch and the griping movements of the uterus post partum.[12] The integration of such findings with the factors present in human toxaemia has been fully dealt with by me elsewhere[6, 13] and an aetiological association thereby provided.

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Items

American Board of Obstetrics and Gynecology, Inc.

The Part II Examinations of the American Board of Obstetrics and Gynecology were held May 12 through 20 at the Edgewater Beach Hotel in Chicago, Illinois. Three hundred eighty-seven candidates were examined.

After twenty-five years of continuous service, Dr. Walter T. Dannreuther was succeeded as President of the Board by Dr. F. Bayard Carter. Dr. Dannreuther will continue with the Board as a member of the Executive Committee.

After many years of faithful service as a Director, the resignation of Dr. Willard R. Cooke was accepted with regret and Dr. Conrad G. Collins of New Orleans was elected to fill his unexpired term.

Applications for certification for the 1956 Part I Examinations are now being accepted. Candidates are urged to make such application as early as possible, and before Oct. 1, 1955.

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Inter-Society Cytology Council

The next meeting of the Inter-Society Cytology Council will be held at the Statler Hotel, Cleveland, Ohio, Nov. 11 and 12, 1955.

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